University of Alberta

The Effects of Load on Normal, Infant and Parkinsonian Human Gait

By

Marilee Jane Stephens ©

A thesis submitted to the Faculty of Graduate Studies and Research in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

Division of Neuroscience

Edmonton, Alberta

Fall 2000

National Library of Canada
Acquisitions and Bibliographic Services
395 Wellington Street
Ottawa ON K1A 0N4
Canada

Bibliothèque nationale du Canada
Acquisitions et services bibliographiques
395, rue Wellington
Ottawa ON K1A 0N4
Canada

Your file Votre référence

Our file Notre référence

The author has granted a non-exclusive licence allowing the National Library of Canada to reproduce, loan, distribute or sell copies of this thesis in microform, paper or electronic formats.

The author retains ownership of the copyright in this thesis. Neither the thesis nor substantial extracts from it may be printed or otherwise reproduced without the author's permission.

L'auteur a accordé une licence non exclusive permettant à la Bibliothèque nationale du Canada de reproduire, prêter, distribuer ou vendre des copies de cette thèse sous la forme de microfiche/film, de reproduction sur papier ou sur format électronique.

L'auteur conserve la propriété du droit d'auteur qui protège cette thèse. Ni la thèse ni des extraits substantiels de celle-ci ne doivent être imprimés ou autrement reproduits sans son autorisation.

0-612-59676-1

Canada

University of Alberta

Library Release Form

Name of Author:	Marilee Jane Stephens
Title of Thesis:	The Effects of Load on Normal, Infant and Parkinsonian Human Gait.
Degree:	Doctor of Philosophy
Year this Degree was Granted:	2000

Permission is hereby granted to the University of Alberta Library to reproduce single copies of this thesis and to lend or sell such copies for private, scholarly or scientific research purposes only.

The author reserves all other publication and other rights in association with the copyright in the thesis, and except as herein provided, neither the thesis nor any substantial portion thereof may be printed or otherwise reproduced in any material form whatever without the author's prior written permission.

Marilee J. Stephens

(Student's signature)

R.R. #1
St. Marys, Ontario, Canada
N4X 1C4

Date Submitted to the Faculty of Graduate Studies and Research: Oct. 3, 2000

University of Alberta

Faculty of Graduate Studies and Research

The undersigned certify that they have read, and recommend to the Faculty of Graduate Studies and Research for acceptance, a thesis entitled The effects of load on normal, infant and Parkinsonian human gait submitted by Marilee Jane Stephens in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

J Yang

Dr. Jaynie Yang
Supervisor

KG Pearson (Chair)

Dr. Keir G. Pearson

RB Stein

Dr. Richard B. Stein

Dr. Arthur Prochazka

Oct 3, 2000

Date

KG Pearson for

Dr. V. Reggie Edgerton
External Examiner

ABSTRACT:

The purpose of this thesis is to determine if the amount of load on the extensor muscles of the leg is involved in determining the stance-to-swing transition during human gait. This transition is a critical period during the step cycle as stability can be compromised if it occurs at an incorrect moment. Studies on reduced animal preparations show that increasing the load input prolongs the stance phase and delays the onset of swing. Healthy adult humans, healthy infants with functionally immature supraspinal descending inputs and neurologically impaired people suffering from Parkinson's disease were studied. Parkinson's patients were included as some patients have difficulty in initiating a step.

The results of this thesis show that changes in load will affect the generation of the walking pattern in humans. The response seen is dependent on the state of the system, the nature of the disturbance and the task at hand. For example, in sitting, electrical stimulation of group I afferents from an extensor muscle cause an inhibition of the activity of a synergist muscle in healthy adults. During walking, the same stimulus causes less inhibition, and in some subjects, it causes facilitation of the synergist muscle. Mechanically loading the extensor muscles during walking results in responses that are dependent on whether the load causes a postural instability. The amplitude and duration of the extensor activity are modified separately to compensate for the changes in load. With increased postural instability, there are changes in the duration of muscle activity. In a posturally stable situation, loading results in minor changes in the duration of muscle activity. The load is mostly compensated for by an increase in the amplitude of the activity of the extensor muscles. This is not the case in the non-independently locomoting infant. Regardless of the method of introducing load, infants respond by prolonging the extensor burst and the step cycle. The ability to modulate the response to load seems to be dependent on functionally mature descending systems. In Parkinsonian subjects, electrical activation of the group I afferents does not seem to affect the output of the soleus motorneuronal pool, either during sitting or walking, though a trend towards facilitation is seen during sitting. However, it appears that this population may use more cortical control during walking as distracting attention away from their walking causes it

to deteriorate. Modulation of the group I pathway is clearly altered in this population, but the mechanisms for the alteration remain unknown.

Dedication:

This thesis is dedicated to my family: William, Anna, Michael, Sandy, Scott and Mark Stephens, for allowing me to be me while encouraging me and providing support to me in my pursuit of this degree.

It is also dedicated to my god-daughter, Tia Giuseppina Bennett, who reminds me every day about what's really important in life: to love and to be happy.

Acknowledgements

There are a number of people I have to thank for the help and encouragement they gave me over the course of this thesis work.

First, I need to extend my greatest thanks to my supervisor, Dr. Jaynie F. Yang, for continuing to support me over the time I spent in her lab. I know that I could be very frustrating at times, and she willing stuck with me through it all.

My supervising committee and thesis committee members also need my thanks, not only for sitting on my committees, but for also providing personal encouragement when I needed it. To Dr. Keir Pearson, Dr. Arthur Prochazka and Dr. Richard Stein, my deepest thanks.

I also need to thank my external examiner, Dr. V.R. Edgerton for taking the time out of his busy schedule to read and comment on my thesis. Especially given the fact that he had a health problem to deal with at the time.

Dr. David Bennett and Dr. Monica Gorassini deserve some of my biggest thanks. They've been my friends, been there for me when I needed it, and taken me into their family. Without them, I would have been lost at times.

Dr. Sophie De Serres also gets my gratitude, for giving me her friendship, but also for writing a number of the computer programs I used to analyze my data.

Dr. John Misiaszek allowed me to work with him on the loading through the long axis of the leg project, and helped me formulate some of the ideas presented in this thesis, as well as provided encouragement when I needed it. Thanks, John.

I have to thank Rosie Vishram for all the help in collecting the data for the projects, as well as being my friend and helping me sort out areas of my life that needed sorting out.

My fellow graduate students in Dr. Yang's lab, Tania Lamb and Marco Pang, provided help, encouragement and places to vent when I needed it.

Toni Stringham and Carol Ann Johnson each get a huge "thank you" from me for handling all the paperwork required to help me complete my degree, as well as providing a friendly ear. They were my "moms-away-from-home" and I appreciate it.

I have to thank Adrienne and Ralph Wright, for being my friends, encouraging me, and giving me a place to stay.

I need to thank the psychiatrists and pyschologists that have helped me deal with my clinical depression over the course of the last few years. Without their assistance, I would have been much worse off.

I want to thank all my fellow graduate students in the Division of Neuroscience, for providing me with encouragement, but also giving me chances to party and chances to blow off steam when I had to.

And finally, all the members of my extended family and my friends back home in St. Marys, Ontario have to be thanked for giving me support and being there when I really needed it.

TABLE OF CONTENTS

Chapter **Page**

1.0 Introduction 1

1.1 Afferent Control of Stance-to-Swing Transition 2
- 1.1.1 Two Hypotheses for Stance-to-Swing Transition 2
  - 1.1.1.1 Hip Joint Extension 3
  - 1.1.1.2 Loading of the Extensor Muscles of the Leg 6
- 1.1.2 Classical Inhibitory Role of Group Ib Afferents 10
- 1.1.3 Reflex Reversal of the Effects of Group I Pathways during Walking 12
- 1.1.4 Mechanical Loading/Unloading of Humans During Walking 15
- 1.1.5 Different Patterns of Locomotion across Species 17

1.2 Supraspinal Input to the Central Pattern Generators for Walking 20
- 1.2.1 Different Effects of Stimuli due to Different Preparations ... 21
- 1.2.2 Effects of Supraspinal Input on Walking 24
  - 1.2.2.1 Evidence for Central Pattern Generators In Humans 24
  - 1.2.2.2 Role of the Brain Stem during Walking 25
  - 1.2.2.3 Role of the Cerebellum during Walking 28
  - 1.2.2.4 Role of the Basal Ganglia during Walking 30
  - 1.2.2.5 Role of the Cerebrum during Walking 31

1.3 Locomotion in Human Infants 34
- 1.3.1 Lack of Functional Maturity of Infant Corticospinal Tract . 34
  - 1.3.1.1 Development of Corticospinal Tract in Lower Mammals 34
  - 1.3.1.2 Development of the Corticospinal Tract in Human Infants 36
- 1.3.2 The Infant Stepping Reflex 39

1.4 Locomotion in Neuropathologies 42
- 1.4.1 Changes in Reflex Modulation in Different Neuropathologies 42
- 1.4.2 Motor and Sensory Deficits Associated with Parkinson's Disease 44
- 1.4.3 Deficits in Parkinsonian Gait 46

1.5 Summary of Contents of this Thesis 51
1.6 References 53

TABLE OF CONTENTS (con't)

2.0 Short Latency, Non-Reciprocal Group I Inhibition is Reduced During the Stance Phase of Walking in Humans.

2.1 Introduction 65
2.2 Methods and Materials 68
2.3 Results 75
2.4 Discussion 83
2.5 References 88

3.0 Loading During the Stance Phase of Walking in Healthy, Adult Humans

3.1 Introduction 91
3.2 Methods and Materials 94
3.3 Results 101
3.4 Discussion 109
3.5 References 116

4.0 The Effect of Transient Mechanical Loading on Infant Stepping

4.1 Introduction 119
4.2 Methods and Materials 123
4.3 Results 131
4.4 Discussion 145
4.5 References 154

5.0 Effects of Group I Afferent Input on Parkinsonian Gait

5.1 Introduction 160
5.2 Methods and Materials 168
5.3 Results 177
5.4 Discussion 192
5.5 References 209

6.0 Conclusions 215
6.1 References 232

List of Figures

Figure:	Description:	Page:
2.1	Amplitude of Control and Conditioned H-Reflexes during Sitting and Walking for one subject	76
2.2	Averaged Ratio of Conditioned/Control H-Reflexes during Sitting for subjects with conditioning inhibition and without	77
2.3	Individual Ratios of Conditioned/Control H-Reflexes for 2 subjects	78
2.4	Average Conditioned/Control Ratios during Sitting, Walking and Contraction	81
2.5	Facilitation of Conditioned H-Reflex during walking in 4 subjects	82
3.1	Diagram of harness arrangements for loading and unloading	97
3.2	Single Subjects and Average responses to sustained loading	102
3.3	Individual subject EMG and FSR profiles to sudden application of load	103
3.4	Single Subjects and Average responses to transient loading	104
3.5	Single Subjects and Average responses to transient unloading	107
3.6	Single Subjects and Average responses to sustained unloading	108
4.1	Infant EMG and foot contact patterns during treadmill stepping	132
4.2	Index of co-contraction during stepping	133
4.3	Stick figures of undisturbed and disturbed infant stepping	134
4.4	EMG and foot contact patterns from single subject during disturbance	136
4.5	EMG, FSR and Goniometer records during disturbance of swing limb in one infant	137
4.6	Durations of Step cycles of left leg before, during and after disturbance of right swing leg	138
4.7	Effect of disturbances in low weight-bearing conditions	140
4.8	EMG and FSR profiles of transient load disturbance	141
4.9	Effect of transient loading on step cycle and stance phase durations, and extensor burst amplitudes and durations	143
4.10	EMG and force plate profiles of loading disturbance	144
5.1	Average UPDRS Clinical Motor Test scores	179
5.2	Comparison of EMG and FSR patterns between young, healthy adult and Parkinsonian patients	180
5.3	Condition/Control H-reflex ratios for two Parkinsonian subjects	184
5.4	Individual and Averaged Condition/Control H-reflex ratios during Sitting for Parkinsonian subjects versus young healthy adults	185
5.5	Individual and Average Condition/Control H-reflex ratios during Walking for Parkinsonian subjects versus young healthy adults	186

List of Figures (con't)

5.6 Comparison of Averaged Condition/Control H-reflex ratios between sitting and walking in Parkinsonian subjects 187

5.7 Effect of Tibial nerve stimulation train on step cycle and its phases' durations 190

5.8 Effect of distracting attention away from walking task in Parkinsonian subject 191

1.0: INTRODUCTION:

Walking requires several muscles across a number of joints to be turned on with a certain magnitude of activity in the proper order. Co-ordination between the limbs must occur to maintain a stable base of support for the body during locomotion. Walking additionally requires the ability of being able to compensate for changes in the environment. Yet, for the most part, walking is an automatic task, with little conscious thought going into maintaining the rhythm and making compensations for perturbations. How the nervous system can accomplish this task with so little demands on conscious voluntary control is a question that has had a large body of study devoted to it.

Both the central and peripheral nervous systems contribute to the control of walking. Peripheral inputs (muscle, tendon, joint, and cutaneous) have been shown to help shape the patterns of the walking pattern, both in terms of timing and magnitude of activation of various muscles (reviewed in Rossignol, Lund and Drew, 1988; Grillner and Debuc, 1988; Pearson, 1993; Buschges and El Manira, 1998). An alternating pattern of extensors and flexors needed for the basic locomotor rhythm can be generated within the spinal cord itself (Grillner and Zangger, 1979). The information from peripheral inputs can be used to adjust this basic oscillatory pattern. When and how the various modalities of sensory input are used may change over the course of the step cycle, with different inputs playing greater roles in one phase of the step cycle than they do at others. Knowing when and how the various inputs are contributing to the patterning of the step cycle is important for understanding the underlying mechanisms that shape locomotion.

An example of when sensory information is important in shaping the locomotor pattern is during the transition from stance to swing during a step cycle. This particular point in the locomotor cycle must be carefully controlled. If the transition occurs at the wrong point, before the other limb or limbs are fully prepared to support the weight of the animal, a fall could occur. Individuals affected with certain neuropathologies (ie. stroke, Parkinson's Disease) have difficulty initiating this transition. Studying what factors influence the generation of this transition and how the deficits found in these neuropathologies affects these control factors may aid in determining how specific afferent input, such as load, plays a role in controlling the locomotor pattern. As well, by examining neuropathologies where descending supraspinal influences are absent or compromised can indicate how the supraspinal centres control or influence the locomotor cycle. Knowledge of the factors that do control the generation of the stepping pattern may also aid in the development of techniques, such as stimulation of certain afferent systems or motor systems, to aid in recovering a proper locomotor pattern in the various neuropathologies.

1.1: Afferent Control of Stance-to-Swing Transition:

1.1.1: Two Hypotheses for Stance-to-Swing Transition:

The focus of this thesis is on the influence of load or tension on the extensor muscles in determining when the stance-to-swing transition occurs during human locomotion. The initial impetus for this series of projects came from results found in animal research. Studies on cats indicated that certain sensory inputs are important for the control of the stance-to-swing transition of the step cycle. Two hypotheses have been put forward in the past as to how peripheral input may be used to dictate when the stance-to-swing transition occurs. The first hypothesis is that the hip angle had to exceed a certain angular displacement (Grillner and Rossignol, 1978). Later work established that this is the result of the hip flexors being stretched and their group Ia afferents activated (Andersson and Grillner, 1983; Kriellaars, Brownstone, Noga and Jordan, 1994; Hiebert, Whelan, Prochazka and Pearson, 1996). The second hypothesis is that the leg will only move into swing when the peripheral afferents register that the load being carried by the limb has decreased. The proposal was that the decrease in tension generated within the extensor muscles, being measured by Golgi Tendon Organs (GTO's), indicated that the leg was not being used to carry as much of the body weight as before. It would therefore be safe for the leg to move into swing. This information would then be transmitted to the spinal cord by group Ib afferents (Duysens and Pearson, 1980). Evidence has been found to support both of these hypotheses.

1.1.1.1: Hip Joint Extension:

Extension of the hip joint, and the resulting stretch of the hip flexors, as a controlling factor in the stance-to-swing transition was originally investigated in spinal cats stepping on a treadmill. When one of the limbs was blocked from moving into extension, the transition to swing did not occur. This lack of swing initiation remained until the leg was allowed to move again, and flexion began when the hip angle exceeded approximately 90 degrees (Grillner and Rossignol, 1978). When ramp stretches of the hip joint were applied during stepping in fictive preparations, different effects were seen dependent on when the stretch was applied during the step cycle (Andersson and Grillner, 1981). When the flexion ramp was applied late during the extensor burst would halt the extension and advance the onset of the flexor phase. If a ramp stretch in the extension direction was applied late in the flexor activity, the flexor burst amplitude was reduced. This extensor ramp stretch increased the size of the extensor burst if applied early in extensor activity.

It has since been shown that low amplitude, sinusoidal movements at different frequencies of the hip can entrain the locomotor pattern in fictive, decerebrate cats (Andersson and Grillner, 1983). This entrainment was due to activation of the muscle afferents (Kriellaars, Brownstone, Noga and Jordan, 1994). Onset of the flexor bursts occurred near the time when the hip was maximally extended in the sinusoidal movements of the hip. The stretch of hindlimb flexors, not just at the hip, but also at the ankle, could cause cessation of stance and a move into swing. Hiebert and colleagues (1996) stretched the hip flexor iliopsoas (IP) and the ankle flexors (TA and Extensor Digitorum Longus) of decerebrate cats while the cats walked on a treadmill. Stretching these muscles during stance reduced the duration of the extensor activity and initiated flexor bursts in the ipsilateral limb. The stretch also caused a decrease in the duration of flexor bursts in the contralateral limb and initiated the extensor bursts in the contralateral limb. Investigating the threshold of activation of the afferents needed to cause this resetting via electrical stimulation of the nerves, it was found that the EDL caused resetting at group I threshold levels, but TA needed stimulation intensities suggestive of group II afferent involvement. This was also true when vibration was applied during stance to the muscles, as vibration of IP or EDL caused the extensor burst to shorten, while vibration of TA didn't affect the locomotor pattern. Very few effects were seen if the various perturbations were applied during the flexion phase of the step cycle. There was no resetting to extension when the flexors were stimulated during flexion, and only stimulation of EDL at higher intensities of stimulation cause the flexor burst to be prolonged if applied in flexion.

Some work has also examined how higher intensity stimulation (group II level and up) of the flexor nerves will affect the locomotor pattern. Perreault and colleagues (1995) examined how electrical stimulation of the hindlimb flexor nerves affects the fictive locomotor pattern in decerebrate cats at stimulation intensities of 2-5 times threshold. They stimulated the TA, Posterior Biceps and Semitendinous or the Sartorius nerve afferents for short trains (20-50 stimuli at 100 Hz). Stimulation of one of these nerves at 5 X threshold during the flexion phase caused a termination of the activity in the flexor nerves and an onset of activity in the extensor muscles' nerves. Stimulation of the TA or PbSt nerves at this intensity during the extension phase resulted in no perturbation of the locomotor cycle. Stimulation of the Sartorius nerve at this intensity during extension resulted in a prolongation of the extensor phase. Stimulation at 2X threshold during the flexion phase of the Sartorius or PbSt did not cause a resetting of the step cycle. This suggested that group II afferents must be responsible for the resetting seen at 5X threshold stimulation intensities. Stimulation of the TA afferents at 2X threshold did cause a resetting. The authors felt that this might be due to the TA having a high percentage of low threshold group II afferents. Stimulation of joint and cutaneous nerves at group II strength did not cause any effects. These results differ slightly from those found in fictive locomotion induced in spinalized cats (Schomberg, Petersen, Barajon and Hultborn, 1998). There, stimulation of flexor reflex afferents (FRA) of the proximal joints, which include joint, cutaneous and group II and III muscle afferents, caused a resetting of the locomotor rhythm that was mainly characterized by a flexion reflex pattern. With stimulation of these afferents during the extension phase, the extersor activation was interrupted and a flexor phase was initiated. If stimulated during the late flexion phase, the flexor activity was prolonged. By focussing on a particular nerve branch, the investigators could determine the resetting strengths required for the different types of nerve afferents. Activation of cutaneous nerves could reset the rhythm with a stimulation intensity as low as 1.1 X threshold. Joint afferents could reset the rhythm at 1.6 to 2.2 X threshold. The flexor and extensor at the hip tended to need somewhat higher stimulation intensities (2.4 to 5 X threshold). However, stimulation of the nerves to the more distal extensors or the sural nerve during the extension phase would prolong the extensor activity, and if done during late flexion, would terminate the flexor activity and initiate extension. The authors felt the results found with the distal extensors were due to concommitant stimulation of group I afferents, or in the sural nerve, non-FRA pathways. It was mentioned these results could differ from those seen in the decerebrate cat preparation due to the fact that descending inputs could be inhibiting the efficacy of the FRA pathways. Still, the results of these studies show that flexor afferents can play a role in determining the stance-to-swing transition.

1.1.1.2: Loading on the Extensor Muscles of the Leg:

The second hypothesis was that the amount of weight being carried on the stance limb determined when the stance-to-swing transition occurred. In mammals, this concept was developed from work on the decerebrate cat, where one leg was denervated except for the Triceps Surae and Tibialis Anterior (TA) muscles. The limb was rigidly fixed in a frame, where the hip was held extended (135 degrees), the knee positioned at 140 degrees and the ankle held at more than 90 degrees. The other legs were allowed to walk freely on the treadmill. When the other limbs were walking, rhythmic bursts in the ankle flexors and extensors could be recorded in the fixed leg. However, when the Triceps Surae was stretched, such that the force of the contractions exceeded 40 N, the rhythmic contractions stopped. They only restarted after the force generated in the stretched Triceps Surae fell below 40 N (Duysens and Pearson, 1980). Since it was the level of tension in the extensor muscle, and not the length of the muscle, that consistently indicated when the flexor bursts would reappear, input from the group Ib afferents were thought to control this transition. Further work has showed that the locomotor pattern could be reset in fictive, decerebrate cats when the group I afferents from the ankle and knee extensors are electrically stimulated. When the afferents from the extensors were stimulated during flexion, the flexor burst was terminated and generation of an extensor burst initiated. If the stimulus was given during extension, then the extensor burst duration was increased and the flexor burst was delayed (Guertin, Angel, Perreault, and McCrea, 1995). From intracellular recordings in a spinalized, fictive cat preparation, the termination of the flexor bursts was shown to be due to a rapid hyperpolarization of the flexor motorneurons. This hyperpolarization appeared to be the result of a disfacilitation of the flexors, as when the stimulus was given during a period of flexor inactivity, no membrane potential shift was seen, indicating that it was not a post-synaptic effect. Therefore, it appeared that the extensor group I afferents (with the probability being group Ib's) have access to the central rhythm generators that control the walking pattern (Conway, Hultborn and Kiehn, 1987). Entrainment of the pattern was also found solely with contractions of the ankle extensor muscles themselves, as long as the contractions produced greater than 10 N of force (Pearson, Ramirez and Jiang, 1992). Thus, it is quite apparent that a drop in the tension generated within the extensor muscles of the leg, and particularly the ankle, is one of the necessary conditions for allowing the leg to move from stance to swing. This makes sense functionally, as the animal would not want to move the leg into swing if the limb is supporting a large amount of the animal's weight.

It should be noted that load information on the leg is not solely carried by group Ib afferents. It has been shown in thalamic cats that cutaneous afferents from the pad and plantar surface of the foot can also signal increases in load (Duysens and Pearson, 1976; Duysens, 1977). In these studies, afferent input from the sole of the foot was increased, through either electrically stimulating at low intensities the surface of the foot or the nerves that carry the afferent signals from this area of the hind limb. It was found that this stimulus increased the activity in the extensor muscles of the ankle in both amplitude and duration if the stimulation is applied during the stance phase of walking. The subsequent flexor activity was delayed in activation.

Similar effects of load and its afferent inputs on locomotor patterns have been found in other animals. A recent review gives a comprehensive overview of the work done investigating the effects of load on the locomotor systems of both invertebrate and vertebrate species (Duysens, Clarac and Cruse, 2000). A decrease in load, as monitored by the force receptors located on the cuticle of the leg of the cockroach is needed for swing to be initiated (reviewed in Pearson, 1976). It been found in the crayfish that when a limb is placed under load, the stepping frequency decreased and the time spent in the stance phase of the step cycle increased, with corresponding increase in the anterior depressor muscle (an extensor muscle) activation (Grote, 1981). Thus, it appears that the influence of load on prolonging the stance phase of the step cycle is found across several different families of animal species.

Load also seems to have similar effects on other motor tasks besides locomotion. Both in quiet standing in intact cats (Pratt, 1995) and during fictive scratching in decerebrate cats (Perreault, Enriquez-Denton, and Hultborn, 1999), activation of extensor group I afferents caused increased excitation to the other extensors in the hindlimb. Pratt (1995) had intact cats stand stationary with each paw on a moveable transaxial forceplate. She used short trains of stimuli (200 Hz, 20 ms), through intramuscular electrodes implanted in extensors at the hip (Gluteus and anterior Biceps Femoris), knee (Vastus Lateralis) and ankle (Lateral and Medial Gastrocnemius and Soleus), to cause a weak contraction in one or another of these muscles. It was found that stimulation of one of the ankle extensors would cause excitation in extensors and the flexors at the hip and ankle, but not at the knee. However, stimulation of MG or LG would cause inhibition of the Soleus, while exciting the other ankle extensors and the hip extensors. Stimulation of one of the hip extensors caused excitation of the other extensors at all three joints. Onset of EMG responses to the stimulation occurred at a 25-30 ms latency. Since monosynaptic group Ia responses would have been seen at about 10 ms, the author felt that the responses had to be disynaptic or polysynaptic in origin. It should be noted that the effect of mechanical loading was also studied in this preparation. To increase load on the left hindfoot, the forceplate under the left forefoot or the right hindfoot was dropped 40 mm. The reflex responses to this mechanical stimulation were very similar to that seen with LG or MG intramuscular stimulation, as there was widespread excitation of the extensors and flexors at the hip and ankle, with an inhibition of Soleus activity. Pratt concluded from the results that extensor group I afferents (particularly group Ib) contribute to the organization of postural responses evoked by perturbations of the support surface and reflex reinforcement of weight support during stance.

In the study by Perreault and colleagues (1999), they stimulated extensor afferents and recorded post-synaptic potentials in antidromically identified extensor motor neurons in a decerebrate cat preparation during both fictive locomotion and fictive scratching. They found that extensor group I afferent input could alter the timing and amplitude of extensor activity in fictive scratching as seen in fictive locomotion. Group I afferent stimulation could reset the scratching activity if done during the flexion phase by stopping the flexion burst and initiating the extensor burst. If done during extension, the extensor activity was prolonged and the flexion onset delayed. The results of both this study and the previous study by Pratt indicate that it is not only during locomotor activity that the excitatory interneuron pathway acts from extensor group I afferents to extensor motorneurons.

1.1.2: Classical Inhibitory Role of Group Ib Afferents:

Early research established that the reflex connections between the group Ib afferents and the motorneuronal pools of the homonymous muscle and its synergists were inhibitory and disynaptic in nature. Studies done on the cat in static conditions (Laporte and Lloyd, 1952; Eccles, Eccles and Lundberg, 1957) showed this by examining the effects of activation on group Ib afferents on the motorneurons of various muscles. Stimulation of the group Ib afferents caused the generation of inhibitory post-synaptic potentials (IPSP's) in the motorneurons of the homonymous and synergist muscles. It also found there was a corresponding polysynaptic connection to the homonymous muscle's antagonists that was excitatory in nature in spinal cats.

Research has been done in humans to corroborate the idea that activation of the group Ib afferents is inhibitory to the muscle of origin and its synergists. It appears that the afferents from the Medial Gastrocnemius nerve (MG) have few, if any, group Ia connections in the primate to Soleus motorneurons (Hongo, Lundberg, Phillips and Thompson, 1984). When examining the effect of stimulating the MG nerve while the Soleus maintained a tonic background contraction during sitting, an inhibitory period in the Soleus EMG was found occurring with a latency of approximately 40 ms following the MG nerve stimulation (Bouaziz, Bouaziz and Hugon, 1975). The authors felt that this latency could be indicative of a disynaptic pathway being activated, and the inhibition being group Ib in origin. Mao and colleagues (Mao, Ashby, Wang and McCrea, 1984) found similar results when examining the effects of MG afferent stimulation on the Post-Stimulus-Time-Histogram (PSTH) of a soleus motor unit. In 11 subjects, no facilitation was found with stimulation of MG afferents at around motor threshold on the soleus PSTH, while in 3 of these subjects, an inhibition in the activity of the Soleus motor unit output was detected. This inhibition in the three subjects lasted approximately 7.8 milliseconds. A condition-test paradigm was developed where the MG nerve was stimulated at group I strength at various time intervals prior to a Soleus H-reflex being generated. Using this paradigm, it was found that the magnitude of the H-reflex was inhibited when MG nerve stimulation preceeded the Tibial nerve stimulation at certain time intervals. These time intervals were consistent with a disynaptic connection (Pierrot-Deseilligny, Katz and Morin, 1979). Therefore, in the static case, afferent information from the

GTO's does appear to be inhibitory to a muscle's synergists in humans.

1.1.3: Reflex Reversal of the Effects of the Group I Pathways during Walking:

Though the effect of the group Ib afferents may be inhibitory in the static case, the effect of a reflex pathway may be modified with different tasks, or even reversed from that seen at rest. This switch in the response to the same stimulus is known as a "reflex reversal". Such reversals can also be seen between different phases of a task such as stance versus swing phase of walking (cutaneous: cat: Forssberg, Grillner and Rossignol, 1975, 1977, human: Kanda and Sato, 1983, Yang and Stein, 1990). Evidence from the cat indicates that a task-dependent reflex reversal might occur for the effects for the group Ib afferents between rest and walking. It has been shown that there are no group Ia connections between Plantaris and MG, two extensors of the ankle, in the cat (Eccles et al, 1957). Taking advantage of this anatomical arrangement, the effects of the group Ib afferents during walking can be studied. Stimulation of the plantaris nerve during walking caused a strong facilitation of the MG muscle approximately 40 ms after the onset of the stimulus (Pearson and Collins, 1993). Studies of this stimulation at the motorneuronal level show that at disynaptic latencies, in immobilized spinalized cats during walking, the inhibition seen at rest is reduced, while in immobilized decerebrate cats, an excitation is generated (McCrea, Shefchyk, Stephens and Pearson, 1996). These effects were seen especially when stimulation occurred during the stance phase while walking. At longer, polysynaptic latencies (10-40 ms), these reversals were seen at the motorneuronal level in decerebrate and spinalized cats, as the IPSP's generated within motorneurons with stimulation of group Ib afferents during rest became excitatory post-synaptic potentials (EPSP's) (Gossard, Brownstone, Barajon and Hultborn, 1994; Angel, Guertin, Jimenez, and McCrea, 1996). The effects at the longer latencies were stronger during the flexor phase. It appears that the interneurons mediating the switch to excitation with group I stimulation in the ankle extensors are found in Lamina VII of the L7/S1 spinal cord (Gossard et al., 1994).

It is interesting to note that the differences between the effects of activating the disynaptic pathway and the polysynaptic pathway are seen in a motor task besides walking. In the study done on decerebrate cats with both fictive scratching and fictive locomotion, Perreault and colleagues (1999) found similar results during fictive scratching. Recording from extensor motorneurons, they found disynaptic EPSP's were generated with stimulation of ankle extensor afferents (3-5 Hz, 1-3 pulses at 100-300 Hz) during the extensor phase of the fictive scratching cycle in approximately 60% of the extensor motorneurons studied. Polysynaptic EPSP's were evoked more often in the flexion phase of the scratching cycle with the stimulation of the ankle extensor afferents.

The functional significance of this reflex reversal during locomotion is that a positive force-feedback loop would be established so that as long as the extensor muscles are generating a sufficient amount of force, this loop would reinforce a continued activation of these synergists. In fictive locomotion in both decerebrate and spinalized cat preparations, it was found that stimulation of knee and ankle extensor group I afferents caused oligosynaptic excitation of the extensor motorneurons. If applied during flexion, it removed the depolarization of the flexor motorneurons and caused EPSP's to be generated in the extensor motorneurons. During extension, smaller EPSP's were evoked, with no apparent effects on the flexors (Gossard et al., 1994). During active locomotion, stimulation of extensor afferents at group I levels, when applied during stance, prolonged the extensor bursts and delayed the onset of flexion in decerebrate cats. This occurred even with long trains of stimulation. When stimulated during flexion, the activation of the extensor afferents caused an abrupt termination of the flexors' bursts and a resetting to extension until the stimulation was over, at which time swing would start again (Whelan, Hiebert and Pearson, 1995).

While the increase in extensor activity has mainly be attributed to a reflex reversal in the actions of the group Ib pathway, there has also been evidence that some of the extensor activation is due to group Ia afferents. It has been found in fictive preparations that selective activation of group Ia afferents from ankle extensors by muscle stretch also causes increased extensor activity via a disynaptic pathway (Guertin et al., 1995).

It had been shown in intact cats (Gorassini, Prochazka, Hiebert and Gauthier, 1994) that when a cat's foot encounters a hole while walking, there is a rapid flexion of the leg out of the hole and replacement of the foot on the ground. A similar response was seen in spinalized cats, though somewhat slower in onset and with a weaker activation of the flexors (Hiebert, Gorassini, Jiang, Prochazka and Pearson, 1994). Decerebrate cats also showed this flexion response. However, with extensor afferent nerve stimulation, the leg remained in extension and in the hole, even exceeding the duration of the stimulus trains (Hiebert, Whelan, Prochazka and Pearson, 1994). Thus, it appears that unless there is group I afferent input to the spinal cord, especially that of the group Ib's indicating the limb has regained support, the limb will initiate the flexor response. Therefore, the evidence suggests that during locomotion, group Ib afferents from extensor muscles of the leg change from having an inhibitory influence on homonymous and synergistic muscles, to having a facilitating influence.

The first study in this thesis investigated whether the reversal in the effects of group Ib afferent stimulation also occurs in human locomotion (Chapter 2). This was studied by examining the effect of extensor afferents from a single extensor (MG) onto another extensor (soleus) during both relaxed and contracted static conditions and during the mid-stance phase of the step cycle.

1.1.4: Mechanical Loading/Unloading of Humans during Walking:

If the load sensitive afferents truly have the functional role of adjusting the step cycle as suggested (initial hypothesis of Duysens and Pearson, 1980), then one would expect the response to real loads added to a walking subject to reflect this. Several studies have investigated the effects on the extensor muscles' activity when a person is lifted slightly in a harness while walking on a treadmill. This results in a decrease in the amount of body weight the extensor muscles are supporting during the stance phase. As the subject had to support more of the body's weight as s/he was lowered in the harness, the amplitude and duration of the extensor muscles' EMG bursts increased. As well, there are increases in the percentage of time the leg will remain in stance, and increased double support time between legs (Finch, Barbeau and Arsenault, 1991; Harkema, Hurley, Patel, Requejo, Dobkin and Edgerton, 1997). Several studies have also looked at what happens when load is added to a person's normal body weight when walking. It has been found that with these increases in load, normal humans will decrease their stride length, while the percentage of time spent in stance and double support increases (Eke-Okoro and Larsson, 1984). Also, loading causes increased duration of some of the extensor muscles of the leg (Ghori and Luckwill, 1985, Neumann and Cooke, 1985). While these results all agree with the results found in the animal studies, it should be noted that these studies all had some confounding influences. In the unloading studies, removing body weight meant lifting the subject slightly in the harness. While a change in the timing of the step cycle does indicate that there is a change in the output signals from the CPGs, the signal that initiated this change in CPG output is not clear. Afferent signals would indicate that there is less or more load being placed on the extensor muscles of the leg. However, there is the possibility of a confounding mechanical factor in that the slight lifting could cause a shortening of the stance duration as the contact area on the treadmill that the leg can reach will be shortened by the lift. A counter argument to that possibility is certain studies that have been done using a harness that has some compliancy built into it though the use of springs to lift the subject, which simulates reduced gravity yet allows for longer contact periods with the treadmill surface. Reducing the gravity still caused decreases in stride length when studied during gait with constant Froude numbers (Donelan and Kram, 1997). The Froude number is a dimensionless ratio comparing centripedal to gravitational forces, and is calculated using velocity, gravity and the subject's leg length. In conditions with a constant Froude number but different amounts of gravity, the "duty ratio" (stance duration/step cycle duration) remained nearly a constant value. When walking at matched speeds, the duty factor and relative stride length decreased with reduced gravity (10% and 16% respectively). In this particular study, the mechanical factor was not a problem. However, as a person is lifted during the unloading, it is difficult to determine what is causing the stance-to-swing transition during the gait cycle. Possibilities could include the fact that there is reduced load being carried on the leg, or that the cuntaneous input from the foot is decreased as the leg moves back into extension. Even cutaneous input at the hip, due to the harness about the upper part of the thighs, could play a role. When the load is being replaced, by re-weighting the person, the increased stance time could be due to the leg remaining in contact with the surface of the treadmill longer with more cutaneous input from the foot, or the input from the hip region differs. The magnitude changes seen in the amplitude of the extensor EMG are probably due to changes in the amount of load being placed on the limb though, as with the body carrying less weight, the amount of force required to push the body up and forward would be less. In the loading studies, the load was applied either by being carried in the hands or in a pack on the back. Thus, the increased weight would not be uniformly distributed around the Centre of Mass (CofM) of the body, and some of the changes seen might be due to the changed postural requirements, as opposed to just the increased load.

In the second study of this thesis (Chapter 3), we developed a loading paradigm that allowed a load of 30% body weight (BW) to be applied or removed in a manner that allowed for equal distribution around the CofM. This removed the confounding postural problems of previous studies. Another paradigm developed allowed for loading of approximately 60% BW along the long axis of the leg in late stance.

1.1.5: Different Patterns of Locomotion across Species:

Most of the research examining the mechanisms that control locomotion has been done on reduced animal preparations. To what extent the same mechanisms are used in human locomotion is not completely clear. When investigating these mechanisms, two factors must be considered. These factors are the effect of the various preparation techniques, with removal of a variety of different inputs that do play roles in normal locomotor patterning, and the differences in the actual gaits seen in different animal species.

There is the obvious distinction of biped versus quadrupedal locomotion between humans and most of the mammals that have been used in investigating the mechanisms that control walking. This is a large distinction from a biomechanical standpoint. One of the mechanical principles that accounts for a body's ability to remain stable against external forces is that maintainence of stability is proportional to the area of its base of support (Hayes, 1982). Walking on four limbs allows for a larger base of support for the moving mass of the animal to be situated over. Human bipedal locomotion is a different task posturally as there is a relatively large percentage of the body mass situated over a proportionally smaller base of support at a greater distance (ratio of body height) above the support surface. Approximately two-thirds of the body mass is situated in the upper body (head, arms, trunk and pelvis) (Winter, 1991). The centre of mass of the body (C of M – a hypothetical point location that represents the total mass of the body) is situated approximately two-thirds body height above the ground. The position of the C of M changes according to the movements and positions of the individual body segments (Murray, Seireg and Sepic, 1975). With locomotion, the C of M for humans tends to fall outside the base of support. As another mechanical principle for the maintanence of stability is that stability is directly related to the horizontal distance of the C of M to the edge of the base of support (Hayes, 1982), bipedal human walking requires a large degree of control to keep the body upright while walking.

As well as the relatively obvious difference in terms of the number of support limbs, human locomotion differs from quadrupedal walking in terms of the actual kinematics and electromyographic activation seen. A review by Vilensky (1987) outlines how human, non-human primates and quadrupedal mammals differ in terms of their locomotor patterns. One difference is in the fact that most quadrupeds walk with a digitigrade gait pattern (the footfall is on the toes). Humans, once the locomotor pattern is mature (see later sections in this introduction) walk with a plantigrade gait (initial footfall is on the heel). This plantigrade gait is seen in walking and slow running. When running at higher speeds, digitigrade gait is seen.

The kinematics of the gait patterns are also different in that in the quadrupedal mammals most commonly studied (cats and dogs), the angular displacements of the three joints of the limb (hip, knee and ankle) tend to work in phase for middle and late stance and most of swing. The hip tends to be out of phase with the knee and ankle for early stance (cats: Goslow, Reihking and Stuart, 1973; dogs: Wentik, 1976). This is different from humans, where the knee and ankle during the stance phase of walking tend to operate out of phase (Pierrot-Deseilligny, Bergego and Mazieres, 1983). Even at a single joint, the angular excursion can be different between quadrupedal and human bipedal walking. In the quadrupeds, a period of both flexion and extension is seen during each of the stance and swing phases of the step cycle in the ankle joint (Grillner, 1981). In human walking, the ankle's angular excusion shows only flexion during the swing phase, and extends, flexes and then extends again during stance (Nilsson, Thorstensson and Halbertsma, 1985). These differences between quadrupedal and human bipedal walking in terms of the coordination between the joints during walking may indicate that certain aspects of the control mechanism controlling walking is different between the two types of gait.

Vilensky (1987) provides a clear overview of the noted differences between activation patterns for the muscles used in walking between non-primate quadrupeds and humans. The main ones mentioned was in terms of activation of the gastrocnemius and tibialis anterior at the onset of stance. In quadrupeds, the Tibialis Anterior is active solely during swing. In human walking, there is also a burst at the end of swing/beginning of stance phase that is used to help lower the forefoot to the ground after the heel hits the ground. As quadrupeds walk with a digitigrade pattern, this burst is not required. Gastrocnemius activation varies, as quadrupeds tend to have these muscles active at foot-strike, while in humans, activation is not seen until later in the stance phase.

However, overall muscle activity is preserved in the various species, with extensors mainly activated during stance, and flexors during swing. Vilensky (1987) noted one other similarity between human walking and quadrupedal gait in terms of single limb mechanics. In both quadrupeds and humans, with increased speed, stance duration decreases while swing duration remains relatively stable. But there must be some differences in the activity of the spinal circuitry for walking to accommodate the differences between the species in terms of their different gait requirements.

1.2: Supraspinal Input to the Central Pattern Generators for Walking:

From the studies outlined above, it is obvious that sensory mechanisms are important in the generation of the walking pattern. However, other work has shown that higher centres are also used during walking. With higher centres of the nervous system intact, changes can be seen in how the animal will react to a specific given stimulus.

1.2.1: Different Effects to Stimuli due to Different Preparations:

Recently, evidence from animal work has indicated that the amount of influence the higher centres have on the spinal cord may modify the effect of peripheral influences on the walking pattern. A given stimulus might not have the same effects in a spinalized cat versus one who is walking intact. In looking at the effects of loss of ground support under the leg, it has been seen that the corrective flexor response was stronger and faster in intact animals than that seen in spinalized or decerebrated cats (Hiebert et al., 1994; Hiebert et al., 1995). In both the spinalized and decerebrate cats, the response to the loss of ground support by the ipsilateral hindlimb stepping into a hole resulted in a flexor response that occurred approximately 200 ms after the foot passed through the hole. The magnitude of the flexor bursts was similar to the activity seen in a normal swing cycle. It was usually not enough to lead to regaining support on the treadmill belt, and often would be followed by a further extension back into the hole, and a second burst of flexor activity. In intact cats, however, the flexor bursts were initiated approximately 100 ms after the foot entered the hole, and the magnitude of the bursts was greater than that seen during a normal swing phase, allowing for a large flexion out of the hole and regaining limb support with one attempt. The authors believed these differences were due to supraspinal centres facilitating spinal pathways that carry the novel sensory signals produced when the foot enters the hole, or that the novel sensory signals are acting via a supra-spinal pathway to facilitate the flexion effect.

It has also recently been seen that in different preparations, increasing load on the hindlimbs, via electrical activation of the group Ib afferents or mechanically loading the limbs, may have slightly different effects on how the stance phase is effected. In spinalized cats, activation of the group Ib afferents has been shown to reset the locomotor pattern (Conway et al., 1987, Pearson et al., 1992). In walking decerebrate cats, electrical stimulation of group Ib afferents from the extensor muscles prolonged the stance phase and the extensor burst of the step in which the stimulus is applied for the duration of the stimulus, even for very long trains of stimulation (>600 ms). However, it does not tend to reset the pattern, as the following step will be shortened to compensate for the increased duration of the previous step (Whelan et al., 1995). There was also a modest increase in the duration of the contralateral limb's subsequent step. When examining the effects of these same stimuli trains in the intact animal, the results were much more modest and variable than those seen in decerebrate animals were (Whelan and Pearson, 1997). The extensor bursts did not necessarily last for the duration of the stimulus train. On average, the step cycle duration was only increased by less than 14%, whereas in the decerebrate cat, the cycle duration might increase by more than 100%, dependent on the nerve stimulated and the length of the stimulus train. It was also found that in decerebrate cats, increasing the stimulation to the MLR that was used to produce walking would decrease the effects of the extensor afferent stimulus on prolonging the stance phase. As well, the authors found that when the stimulus was applied during biped walking (the hindlimbs walked on the treadmill while the forelimbs were stationary on a platform) that a greater effect was seen than that seen during quadrupedal walking. An 18% increase in step cycle was found with stimulation during bipedal walking versus a 9% increase during quadrupedal walking. The authors though this difference may be due to influence from the forelimb locomotor centres that wouldn't be present during bipedal walking. Therefore, it appears that greater supra-spinal input and centres higher in the spinal cord does influence the degree to which peripheral input may affect the durations of the stance phase and step cycles.

Differences in the effects of group I afferent stimulation between various preparations can also be detected at the motorneuronal level (McCrea et al., 1995; Angel et al., 1996). When stimulating group I afferents during locomotion in fictive preparations of decerebrate cats walking with stimulation of the MLR, it was found that the disynaptic IPSP's generated during rest were replaced by disynaptic EPSP's during the extensor phase of locomotion. During flexion, neither disynaptic IPSP's nor EPSP's were generated. The same stimulation was applied to spinalized cats where fictive locomotion had been generated by application of clonidine and perineal stimulation. However, in this preparation, no disynaptic EPSP's were found, though there was a substantial reduction in the size of the IPSP's generated across all phases of the step cycle.

These studies show how the different types of preparations, with their inherent different degrees of supraspinal input onto the central pattern generator, may allow for differences in how the locomotor pattern is changed with regards to a given stimulus. Therefore, it is important to know how the various higher levels of the nervous system influence the walking pattern.

1.2.2: Effects of Supra-spinal Input on Walking:

1.2.2.1: Evidence for Central Pattern Generators in Humans:

As mentioned, the spinal cord is capable of generating and maintaining a walking pattern, either with or without input from higher centres or the periphery (Grillner and Zangger, 1975). The mechanism that allows for this generation of a cyclic activity appears to be a network of interneurons termed a Central Pattern Generator (CPG) (reviews: Forssberg, 1982, Grillner and Wallen, 1985, Grillner and Debuc, 1988). Grillner describes CPGs as "unit generators" for each separate joint of the limb. The "half-center" model stated that each CPG consists of two separate sets of interneurons, one that controls activation of the extensors crossing the joint and one controlling the flexors, that interact in an inhibitory manner on each other. The CPGs of each limb will communicate with each other and the ones for the other limbs to allow for smooth co-ordination of activity. CPGs have been found in several invertebrate and lower vertebrate species (Review: Pearson, 1993).

Evidence has been found that a spinal CPG may also exist for generating the locomotor pattern in humans. The most direct evidence for this is found in the work of Dimitrijevic and colleagues (1998). In six clinical complete spinal cord patients, they were able to elicit locomotor-like EMG patterns and movements of the lower limb when they applied a train of electrical stimuli through an epidural electrode at the L2 segment of the spinal cord. The step-like patterns were best elicited using stimulation strengths of 5-9 volts and frequencies of 25-50 Hz. Stimulation at any other segments lower or higher in the cord did not elicit the stepping pattern, though tonic or non-locomotor-like phasic activity was generated.

Other indirect evidence has also been found suggesting the presence of a CPG for walking in the human spinal cord. While training patients with complete paraplegia to walk on a treadmill, a gross pattern of activation of the lower limb muscles was found that was somewhat similar to that seen in intact human walking. However, the phasing of the activity was not the same as in normals and the amplitudes of the EMG bursts were reduced (Dietz, Colombo and Jensen, 1994; Harkema et al., 1997). A patient with an incomplete, chronic cervical injury was also found to produce spontaneous strong alternating rhythmic movements of the legs with peripheral input while lying supine in bed (Calancie, Needham-Shropshire, Jacobs, Willer, Zych and Green, 1995). And two patients who had suffered herniation at the ponto-medullary level also demonstrated spontaneous rhythmic alternating flexions of the hip, knee and ankle that would last for short bursts of time and occur frequently before death (Hanna and Frank, 1995). These incidents of step-like activation of the muscles in the absence of supra-spinal input indicate that CPGs do exist within the human spinal cord.

1.2.2.2: Role of the Brain Stem during Walking:

Although the spinal cord can generate a walking pattern, higher centres of the central nervous system may play a role in some aspects of how walking is generated and maintained. Several regions in the brain stem of mammals have a direct contribution to the control of walking. Two of the more important ones are the locomotor regions of the reticular formation, one located in the pons, the other in the medulla. The one most studied is the Mescenphalic Locomotor Region (MLR). Stimulation of this area in decerebrate cats causes locomotor activity. A tonic stimulus to this area will result in a phasic activation of flexors and extensors. These results indicate that timing of the stimulus is not related to the rhythm of the locomotor pattern. The intensity of the stimulation is though, as greater the intensity of stimulation, the faster the walking speed, from a step to a trot to a gallop (Shik, Severin and Orlovsky, 1966). Rats also showed this effect of stimulus intensity (Coles, Iles, and Nicolopoulos-Stournaras, 1989). The MLR appears to exert control over locomotion by activation of reticulospinal neurons. Projections from the MLR synapse on the medioventral medulla, which gives rise to reticulospinal tract axons (Garcia-Rill and Skinner, 1987a). Electrical stimulation or chemical activation (by cholinergic agonists) of this area will elicit controlled locomotion in the decerebrate cat as well (Garcia-Rill and Skinner, 1987b).

There has been some indirect evidence that a MLR area exists in humans. A recent study using single photon emission computed tomography (SPECT) showed that normal walking resulted in a greater activation of the dorsal brainstem, analogous to the area of the MLR in cats (Hanakawa, Katsumi, Fukuyama, Honda, Hayashi, Kimura and Shibasaki, 1999). As well, in a case study of a woman who suffered a hemorrhage in the pedunculopontine area of the brainstem (the anatomical equivalent in humans to the MLR), a resultant inability to stand upright and walk in a normal matter was seen (Masdeu, Alampur, Cavaliere, and Tavoulareas, 1994).

The MLR is not the only area of the midbrain that can cause walking. Electrical stimulation of such areas as the cochlear nuclei, the cuneate nucleus, the substantia grisea centralis and the spinocerebellar tracts can also induce locomotion (Beresovskii and Bayev, 1988). As well, stimulation of different areas of the midbrain in the intact active cat can cause different types of walking (Mori, Sakamoto, Ohta, Takakusaki and Matsuyama, 1989). For example, stimulation of the Dorsal Tegmental Field causes suppression of postural support in the hindlimbs, while the opposite effect is seen with stimulation of the Ventral Tegmental Field. MLR stimulation causes faster walking, while stimulation of the Lateral Hypothalamic Area causes the cats to walk slowly, with the head extended, looking around. Stimulation of the Subthalamic Locomotor Region (SLR) causes initiation of gait in a goal-directed manner, which stimulation of the MLR does not. Therefore, it appears that the brain stem acts in the initiation and termination of gait, the control of the walking speed and various behavioural responses, such as goal-directed walking behaviour versus the generation of rhythmic cyclical walking pattern.

The roles of different pathways from the cerebrum and brainstem to the spinal cord have also been investigated during gait. Activation of different descending pathways has different effects on the hindlimb motorneurons. Stimulation of the vestibulospinal tract from the lateral vestibular (Deiter's) nucleus is generally excitatory to extensor muscles, while activating the medial portion of the pontine and bulbar reticular formation is excitatory to the flexors and inhibits the extensors. The caudal and ventral portions of the bulbar reticular formation have inhibitory effects on both the flexors and extensors. The rubrospinal and corticospinal pathways mainly excite the flexors and inhibit the extensors. When the effects of these pathways are examined during walking in mescencephalic and thalamic cats, during different phases of the step cycle, the effects are generally similar to what is found in the static work. In examining the effects on the lateral gastrocnemius and tibialis anterior muscles during walking, Orlovsky (1972) found that stimulation of Deiter's nucleus during the stance phase generally caused increased LG activation, with little effect on TA. No effects were found during the swing phase. Stimulation of the medial bulbar reticular formation during stance caused a decrease in LG activation, while stimulation at the start of swing increased the TA activation, and caused a slight increase in the LG activation in the next step. However, this stimulation at the end of the swing phase, while causing a slight increase in TA, caused the LG burst in the next step to be greatly inhibited. Stimulation of the red nucleus had no effect on either muscle during stance, while in swing, TA activation was increased. If the stimulation intensity was increased during swing, the TA was even more facilitated, but there was also an inappropriate activation of the LG.

1.2.2.3: Role of the Cerebellum during Walking:

The role the cerebellum plays in the control of walking is not totally clear. Removal of the cerebellum does not prevent walking, though the walking pattern seen in both mescencephalic and thalamic cats is highly uncoordinated with its removal (Orlovsky, 1970a). Most of the uncoordination seen was due to excessive extensor tone in the forelimbs, causing the limbs' movements to be very rapid and low in amplitude of displacement.

This problem with coordination seems to be associated with a lack of modulation of the firing of reticulospinal neurons in the brainstem. It has been shown that the majority of reticulospinal neurons active during locomotion are frequency-modulated to different phases of the step cycle, with higher frequencies of activation seen during swing than in stance. This modulation of firing disappeared if the hindlimb's movements were disturbed. This led to the conclusion that it was afferent information that led to the modulation (Orlovsky, 1970b). The removal of the cerebellum causes this modulation to disappear, such that the reticulospinal neurons fire much more tonically. It appeared that the afferent information that led to the modulation was carried by the spinocerebellar pathways, as opposed to the spino-reticular (Orlovsky, 1970a). Orlovsky also surmised that the cerebellum appears to exert an excitatory influence on the reticulospinal neurons, as the average firing frequency of the reticulospinal neurons decreased without cerebellar input (fewer high frequency neurons being seen).

In examining the firing of the cerebellar nuclei during locomotion, Orlovsky (1972) found that a large number of these neurons were also modulated over the course of the step cycle. Recording from both the intermediate and fastigial nuclei, it was found that the cerebellar nuclei neurons involved in locomotion were activated in "packets", where they would be on during one phase of the step cycle (with frequencies of up to 250 impulses/sec) and quiet during the other phase. A small percentage of neurons were active in both phases, but still modulated, having higher activity during one phase versus the other. When the walking cycle was disturbed, the modulation ceased. In examining the relationship of the firing patterns of these nuclear cells to the firing patterns of the brain-stem nuclei that they synapse on, it was found that the modulation of firing of the intermediate nuclei neurons was replicated in the red nucleus cells giving rise to rubro-spinal axons. The modulation of the rubro-spinal cells disappeared if the cerebellum was removed. The same was true with the firing patterns of the fastigial nucleus and the reticulo-spinal cells. However, the modulation of firing of the fastigial nucleus had little effect on the firing patterns of the vestibulo-spinal cells that they also synapse with, indicating that it is not the main modulator of vestibulo-spinal firing. From all the preceeding work, it appears that the cerebellum plays a role in locomotion in relaying afferent information back to the locomotor-regions of the brainstem to help modify their functions.

More recent work by Mori and colleagues has shown that there is a cerebellar locomotor region (CLR) located in the midline of the cerebellar white matter, including the fastigial nucleus. Stimulation of this area in decerebrate cats supported in a sling evoked walking on a treadmill. Increased stimulation caused assymetrical locomotion. When stimulated concurrently with the MLR, it was found that locomotion could be induced with lower stimulation thresholds than could be by the CLR or MLR alone. Removal of either of these sites does not prevent locomotion for being induced by stimulation of the other site (Mori, Matsui, Kuze, Asanome, Nakajima and Matsuyama, 1999). Therefore, it appears that the cerebellum can also play a role in the initiation of walking as well as relaying afferent information to the brainstem sites previously believed to be the sites for the initiation of walking.

1.2.2.4: Role of the Basal Ganglia during Walking:

The Basal Ganglia structures have outputs to several parts of the cerebrum, brain stem and cerebellum, though no direct connections to the spinal cord. They also receive input from several areas of the higher brain centres. In fact, they appear to be involved with at least five different circuits that link the cortex, thalamus and basal ganglia (Alexander and Crutcher, 1990). One of these loops, the "motor circuit" is made up of inputs to the part of the Basal Ganglia called the Putamen from the motor cortex, the premotor cortex, the supplementary motor cortex and the sensorimotor cortex. These inputs are fed from the putamen to globus pallidus internus (GPi) and externus (GPe), as well as the sub-thalamic nucleus (STN). From the GPi, outputs are sent to the Thalamus, which then send outputs back to the motor cortex, the premotor cortex and the supplementary motor cortex (Alexander and Crutcher, 1990). As well, it has been shown in the cat that there are anatomical connections from the entopeduncular nucleus (the analogue of the primate Gpi: Garcia-Rill, Skinner, and Gilmore, 1981) and the substantia nigra (Garcia-Rill, Skinner, Jackson and Smith, 1983) to the MLR. The Basal Ganglia could therefore possibly affect locomotion either through the higher brain centers of the cortex or via the MLR.

1.2.2.5: Role of the Cerebrum during Walking:

Input from the periphery to the sensorimotor cortex has been studied fairly extensively in locomotion. It has been found that when recording from single neurons in the cortex, most of the cells respond to one type of information during locomotion (ie. light touch, pressure, passive joint movement) (Durelli, Schmidt, McIntosh and Bak, 1978), as happens in other tasks. Therefore, such things as skin and pressure units are activated in stance, but not in swing, while joint units are continuously activated. However, while the joint units are continually activated, different ones would have their highest discharge rates at different phases of the step cycle and thus there appears to be modulated input to these cells over the step cycle. When recording from motor cortex neurons, a large number of these cells show phasic activity that is timed to the step cycle. Armstrong and Drew (1984) showed that a large number of these neurons have discharge rates that increase during walking compared to their normal rest values and have frequency modulations that are time-locked to the step cycle. Some of the cells had discharge rates that had a rough linear correlation to the speed of walking. These changes in discharge rates did not always necessarily correspond to changes in muscle EMG burst magnitude though. When the cats walked on an inclined slope, the magnitude of the

EMG changed, without a change in discharge rate, indicating something besides cortical influence was affecting the EMG (most likely afferent input from the periphery). Individual cells tended to have only one burst per step cycle, with different cells' bursting occurring at different times in the step cycle. Since a number of these effects seem to be phase-dependent, it would appear that a regulation of timing is one component of locomotion the cortex can influence.

Recordings from motor cortex neurons during perturbations of gait showed differences if the perturbation was voluntary or unexpected in nature. Examining their activity when the cat has to walk over an obstacle, there was increased peak discharge in a substantial number of pyramidal tract neurons. This tightly corresponded with large changes in the forelimb flexor EMG activity used to lift the limb over the obstacle (Drew 1988). This is somewhat different than that seen with unexpected gait perturbations, where increases in motor cortex activity were seen at short latencies (as low as 20 ms) following the perturbations (Amos, Armstrong and Marple-Horvat, 1989). These changes in discharge were graded to the extent of the perturbation, with a larger perturbation causing larger changes in cortical discharge frequencies.

When Armstrong and Drew (1985) stimulated the motor cortex and monitored the forelimb EMG during walking, it was found that short trains of 20 μA did cause short latency changes in the normal locomotor pattern. EMG was evoked in muscles not normally active in a given phase of the step cycle, or brief facilitation or inhibition of normal EMG activity occurred. The flexors would have an initial excitation that was often phase dependent, occurring when the muscle was normally active or just about to be active. What effect was seen in the extensors depended on where the stimulus occurred in the motor cortex, as some areas produced excitation in the extensors and other sites produced inhibition. When the duration of the stimulus train was prolonged enough, the step cycle would completely reset to that of the train. All these effects were removed, however, if a pyramidectomy was done. This indicated that the corticospinal neurons might have an effect on the timing of the step cycle, even though it is not necessary to generate the basic rhythmic pattern of locomotion.

Orlovsky (1972) found that stimulation of the corticospinal tract at the pyramids at the end of stance/beginning of swing resulted in an increase in TA activity, with a resultant strong ankle flexion. A strong hip flexion was also noted. However, this was followed by a rapid extension at the ankle, with a concurrent increase in LG activity. If the stimulation occurred at the end of swing, a small enhancement of LG was seen. And if a stronger stimulation was used during stance, the LG activation was depressed and TA was activated, leading to a disruption in the locomotor rhythm.

Recently, there has been work examining the role of the motor cortex in human walking using the magnetic stimulation of the cortex. Magnetic stimulation is a painless technique that will activate neurons in the cortex or spinal column (Barker, Freeston, Jalinous and Jarratt, 1987), as well as peripheral nerves. The effects of transcranial magnetic stimulation were examined in the TA and Soleus muscles under static contraction cases. The cortex was also stimulated during both early swing and early stance during walking to see the effects of the stimulation on the same two muscles. It was found that the motor-evoked potentials (MEPs) in the TA were not different between the contracted static conditions and early swing phase of walking. However, the MEPs in the Soleus during the stance phase of walking were substantially reduced from those seen during the static contraction of the muscle. As well, the MEPs in the TA during the stance phase of walking were enhanced compared to those seen during TA's static contraction, and in a majority of the subjects studied, were larger than those elicited in the soleus during the same stimulation. However, the activation of the cortex with magnetic stimulation did not affect the timing of the locomotor pattern at all. The authors felt that these results indicated that the motor cortex may not be actively involved in the timing of the step cycle. It does appear that the corticospinal tract is closely linked with the circuits controlling the flexor TA activation, but not as linked with those of the extensor, Soleus (Capaday, Lavoie, Barbeau, Schneider and Bonnard, 1999).

1.3: Locomotion in Human Infants:

1.3.1: Lack of Functional Maturity of Infant Corticospinal Tract:

How mature the various connections from the supra-spinal centres to the spinal cord are during the different stages of development in humans is not completely known. But one pathway that has been well studied is the corticospinal tract. It has been examined in a number of animal models, as well as infants and children.

1.3.1.1: Development of Corticospinal Tract in Lower Mammals:

In infant mammals, the connections of the sensorimotor cortex to the spinal cord via the corticospinal tract are not fully developed for several days to several months following birth. In the rat, the axons of the corticospinal tract have reached the pyramidal decussation and the upper cervical cord on the day after birth (Schreyer and Jones, 1982; thoracic by 3 days: Clarac. Vinay, Cazalets, Fady and Jamon, 1998). But they do not reach the sacral segments until several days after birth (6 days: Clarac et al., 1998; 9 days: Schreyer and Jones, 1982). This is different from the other descending tracts, which reach the lumbar enlargement in the embryo or around birth, though they might not be fully developed for several days following birth (Clarac et al., 1998). As well, even once the corticospinal tract has reached a given spinal segment, the axons do not enter the gray matter until 2 days afterwards (Schreyer and Jones, 1982). And it appears that though the connections may be anatomically made by a certain stage of development, they might not be functional at that time. Work done in kittens has shown that intracortical stimulation of the motor cortex does not elicit EMG responses in the face, forelimb and proximal hindlimb musculature until the kittens are approximately 40 days old (Bruce and Tatton, 1980). This occurs despite the fact that the connections between the motor cortex and the cervical spinal cord are present by 20 days of age, as shown by retrograde staining using Horseradish Peroxidase (HRP) (Bruce and Tatton, 1981).

Work in lower primates has shown that several months are needed to make fully functional connections from the sensorimotor cortex to the motor neurons. In macaque monkeys, magnetic brain stimulation of the motor cortex was not effective in eliciting EMG responses in forelimb muscles until 4-5 months of age. The stimulation response threshold needed at this time was very high, and did not fall to the threshold level required in adult monkeys until 6.5 to 8 months of age (Flament, Hall and Lemon, 1992). In the hindlimbs, magnetic brain stimulation took slightly longer to elicit responses, as they did not appear until approximately 6 months of age (Flament, Goldsmith and Lemon, 1992). Full maturation of these connections appeared to occur much later, as it's not until 11 months of age that the conduction velocity of these fibres reached adult levels (Armand, Edgley, Lemon, and Olivier, 1994). In the Rhesus monkey, the connections in the lumbar region appear to become fully functional around 8 months of age (Kuypers, 1962). This was shown by the fact that ablations of the sensorimotor cortex did not affect to the same extent the motor performance of very young monkeys. However, when ablations were done on older infant monkeys (approaching the age of 8 months) the effects became more severe and by 8 months, the deficits seen were like the ones seen in adult monkeys with the same lesions.

1.3.1.2: Development of the Corticospinal Tract in Human Infants.

In the human infant, it has been shown that at term, the lateral corticospinal tract has reached the sacral segments of the spinal cord, while the ventral corticospinal tract is at the lumbar segment levels (Humphrey, 1960). However, though the connections may be present at birth, myelination of the tracts only appears to start at the time of birth and is not complete for at least 2 years (Yakovlev and Lecours, 1967; Brody, Kinney, Kloman and Gilles, 1987). Evidence suggesting that the corticospinal tracts are not fully mature until several years after birth has been found using magnetic stimulation of the motor cortex. Several studies have shown that such stimulation does not produce corresponding EMG signals in the arm muscles of infants of a year old unless a background contraction is being held (Koh and Eyre, 1988; Muller, Homberg, and Lenard, 1991, Nezu, Kimura, Uehara, Kobayashi, Ranaka and Saito, 1997). Motor evoked potentials (MEPs) don't appear in the quiescent lower extremity muscles until approximately 4 years of age (Muller et al., 1991). These studies found that the electrophysiological maturation of the corticospinal tracts, based on conduction velocities and shape of the MEPs, are not complete until 11-13 years of age. As well, the threshold for evoking potentials in the EMG starts at a high value in children and decreases until approximately 16 years of age (Eyre, Miller and Ramesh, 1991).

Indirect evidence supporting the lack of functional maturity in the infant cortico-spinal tract has been discovered when investigating cutaneo-muscular reflexes. In adults, electrical or mechanical cutaneous stimulation of the fingers or toes at non-noxious levels causes a triphasic response in muscles of the upper or lower limb. This triphasic response consists of a short latency excitatory component, followed by a slightly longer latency inhibitory phase and then finally a long latency excitatory response. It appears that the initial excitatory response is spinal in nature, while the longer latency excitatory response originates in the cortex. Support for the origin of the different components of the reflex is found in research investigating the cutaneomuscular reflex that has been done on adults who exhibit mirror movements. These mirror movements in some adults appear to be due to lack of inhibition across the corpus callosum, allowing for transmission from the motor cortex down both ipsilateral and contralateral corticospinal tracts. These adults show the typical triphasic response in the expected arm muscle with cutaneous stimulation. However, in the contralateral limb, the longer latency inhibitory and excitatory components are also generated, while the short latency excitiatory burst, believed to be of spinal origin, is not (Mayston, Harrison, Quinton, Stephens, Krams and Bouloux, 1997).

Since the longer latency components of the cutaneomuscular reflex are dependent on supraspinal input, it is important to note that infants do not tend to exhibit these later responses. Work done by Stephens and colleagues (Crum and Stephens, 1982; Issler and Stephens, 1983; Rowlandson and Stephens, 1985a) has shown that newborn infants only show the initial excitatory burst in the muscles with this type of stimulation in both the upper and lower limb. This short latency excitatory burst is also exaggerated in size when compared with that seen in the adult reflex. As well, in adult humans, the response tends to be restricted to one muscle group (ie. Stimulation of the toes causes a response in TA) while in infants, this stimulation will cause short latency responses in all muscle groups (ie. Stimulation caused synchronous responses in TA, Triceps Surae, Hamstrings and Quadriceps, Crum and Stephens, 1982). As the infant grows older, the second, inhibitory response can be elicited with stimulation within the first year, while the third part of the reflex response (the second excitatory component) is not seen until the second year. In the upper limb, Issler and Stephens (1983) could not elicit the biphasic response in any infant younger than 6 months in age, while the triphasic reflex was not present in any infant younger than 15 months in age. As these two responses develop, the magnitude of the initial short latency excitation also decreases. The reflex does not reach the mature adult pattern in terms of the magnitude of each of the components until 8-12 years of age (Rowlandson and Stephens, 1985a). From these results, the authors concluded that the short latency components of this reflex are spinal in nature, but are affected by a tonic descending input from the supra-spinal centres (and hence the decrease in magnitude of response as the descending tracts matures). The second, long latency excitatory response is generated in the cortex itself, where the stimulus from the fingers or toes send afferent signals to the cortex via the ascending dorsal colunms and the motor response is carried by to the muscle via the corticospinal tract). In support of the argument that it is the matured descending tracts that modulate this response, it has been found in adults who have lost descending supraspinal input, the reflex response to the cutaneous stimulation reverts back to the monophasic response seen in the newborn (Choa and Stephens, 1982). In a case of 15 year old suffering from chronic hemiplegia, the affected side showed the monophasic response, while the unaffected responsed to the stimulation with a normal triphasic response (Rowlandson and Stephens, 1985b).

The lack of a completely functional corticospinal tract can also be indirectly be inferred by the fact that H-reflexes can be generated in the muscles of the hands of infants less than 6 months in age (Thomas and Lambert, 1960, Mayer and Mosser, 1969). These reflexes can not be generated in the hand muscles of normal adults, though they can in the hands of people suffering from an upper motorneuronal lesion, where input from the higher brain centres can be impaired or absent. This may indicate that when supraspinal input is present, some of the spinal reflexes may be suppressed. Since H-reflexes can be generated in the hand muscles of the infants, it may be another indicator that functionally mature supraspinal input is not completely developed at this age.

1.3.2: The Infant Stepping Reflex:

Examining walking in the infant model before full maturation of the corticospinal tract is possible due to the fact that even newborn infants display a stepping reflex. The stepping reflex is a well-coordinated response similar to adult walking seen when an infant is held upright while his feet are allowed to touch a flat surface (Andre-Thomas and Autgarden, 1966). Generally this reflex will disappear by 2 months of age, and supported walking motions will reappear around 8 months of age. However, the reflex can be retained if it is actively practiced past the two-month age (Zelazo, Zelazo and Kolb, 1972; Yang, Stephens and Vishram, 1998).

While the stepping response has several characteristics in common with independent walking, there are also several differences. Newborn infants step with a very flexed posture, such that the chin is dropped towards the chest, the arms are flexed and the hip and knees show excessive flexion. The base of support is narrow, and the foot generally makes contact with the floor with the toes or the flat of the foot, but does not show the plantigrade gait associated with adult walking (McGraw, 1940). In analyzing the kinematics and EMG of the stepping reflex, Forssberg and Wallberg (1980; Forssberg, 1985) found that the swing phase is carried out by a strong hip flexion. Once the foot was on the ground, there was also no forward thrust of the limb seen to propel the body forward. The angular excursions of the three joints appear to be in phase with each other in the young infant stepping response (Thelen and Cooke, 1987). Electromyographic data showed the extensors of the knee and ankle are active during stance, but also some co-contraction activity from their antagonists (Forssberg and Wallberg, 1980; Forssberg, 1985; Thelen and Cooke, 1987). However, there has also been evidence to support the clear alternation of extensors and flexors during this stepping motion (Okamoto and Gott, 1985; Yang, Stephens and Vishram, 1998).

When stepping returns after the inhibitory period of 2-6 months of age, there are differences in the stepping pattern from what is seen in the newborn. With increased postural control, the extreme flexion seen early on is gone (McGraw, 1940). The hip and knee angular rotations are becoming out of phase with that of the ankle, as is seen in adult data (Forssberg, 1985; Thelen and Cooke, 1987). The infants still generally walked with either a digitigrade or flatfoot gait pattern. In analyzing ground-force reaction data, these infants did create a forward propulsive force during the stance phase, which was not seen in the young infant stepping (Forssberg, 1985).

The fact that the stepping response can be elicited right after birth indicates that it is generated by circuitry innate to the spinal cord and/or brain stem and appears to be initiated by input from the periphery. However, these infants can not stand independently or appear to be able initiate the stepping voluntarily. To elicit the stepping response in young infants, there needs to be cutaneous and/or proprioceptive input applied to the bottom of the feet, as the child will step when she is tilted forward and rocked a little from side to side (Martin, 1967). The development of the mature walking response from this initial stepping reflex may be the result of changes to the circuitry as the postural requirements and force generation needed for independent walking develop. Also, the input from descending tracts of the supraspinal centres becomes stronger, which could affect the various connections within the walking CPG circuit.

Since the input from supraspinal centres is not fully mature in the infant, infant stepping may be a possible human model that is comparable to the reduced animal preparations that have been used in the past to examine the control mechanisms for walking. How the supraspinal inputs affects the generation of the step cycle can be examined by investigating how different perturbations affect the stepping patterns in human infants compared to the effects of the perturbations seen in adult human walking, where the connections to the spinal circuitry is fully mature. Greater supraspinal input on the interneurons making up the CPG may be one factor that could contribute to afferent activity having modified effects as the central nervous systems matures between the infant and adult states. Other possibilities do exist, such as changes within the connections between neurons at the spinal cord level. Results of the infant study (Chapter 4) indicate that load does have an effect on the generation of the step cycle, though the magnitude of the loading effect in terms of timing of the walking pattern seems to be decreased when an intact supraspinal influence is present.

1.4: Locomotion in Neuropathologies:

1.4.1: Changes in Reflex Modulation in Different Neuropathologies:

It appears that an intact supraspinal system might result in a decreased effect in how changes in load can affect the timing of the walking pattern generated by CPG's. It is therefore possible that this afferent input has a greater effect in how the stance-to-swing transition is regulated in neuropathologies where supra-spinal influences are removed or modified from the normal. It is already known that responses of several reflexes are modified with different types of neurotraumas and neuropathologies, where descending input to the spinal cord is either completely or partially disrupted (ie. complete and incomplete spinal cord injuries, stroke, multiple sclerosis). A large amount of work has been done examining how reflexes are modified with spasticity especially, which may result from a variety of acute or chronic neurotrauma or neuropathologies. Monosynaptic reflexes to perturbations, which may be suppressed in normal gait, appear to be enhanced in spastic gait, while polysynaptic responses are reduced (Berger, Horstman and Dietz, 1984). Also, normally, the soleus H-reflex is modulated during walking such that, with a constant stimulus level (as monitored by the M-wave), the magnitude of the H-reflex increases with greater soleus activation during stance, while it disappears during swing (see Stein, Yang, Belanger and Pearson, 1993). However, in a spastic limb, with the same amount of stimulation, this modulation disappears, though it can be seen if the stimulation intensity is reduced (Yang, Fung, Edamura, Blunt, Stein and Barbeau, 1991). Sinkjaer and colleagues found that the impaired modulation that is seen in spasticity varies with the level of excitation of the muscles, whereas in normal gait other factors contribute (such as presynaptic inhibition) (Sinkjaer, Toft and Hansen, 1995). The interesting thing with this lack of modulation of the Soleus H-reflex in spastic patients during walking is that it can be partially recovered with a conditioning stimulation of the medial plantar nerve, which carries both cutaneous and muscle afferents from the foot. While in normal subjects, this conditioning stimulus cause inhibition of the H-reflex magnitude during all phases of the step cycle, in spastic patients, it caused inhibition during early stance and swing phases. This produced a near normal pattern of modulation of the Soleus H-reflex (Fung and Barbeau, 1994).

Modulation of some cutaneous reflexes is also changed with injury. In incomplete spinal cord patients, it has been found that the medium latency reflexes generated in muscles around the ankle by stimulation of the posterior tibial nerve at the ankle (a mixed nerve with cutaneous afferents and efferents to the muscles of the foot) generally are modulated (Jones and Yang, 1994). However, they are modulated in a different pattern than those that had been previously found in normal subjects. In normal subjects, the responses evoked in the TA by stimulation of this nerve undergo a reflex reversal dependent on the phase of the step cycle they are generated in. During mid-swing, they tend to be excitatory, while in the swing-to-stance transition, they are inhibitory. There doesn't appear to be any reflex response generated during stance. In the soleus muscle, the response to the stimulation tends to be inhibitory during stance, with no effect of stimulation seen during swing (Yang and Stein, 1990). However, in a large number of incomplete spinal cord patients, the inhibitory responses at the swing-to-stance transition in the TA to this stimulation at the medium latency disappear or become excitatory in nature. As well, an excitatory response during the swing phase is seen in the soleus muscle, as well as a possible switch from the inhibitory response seen during stance to an excitatory one.

1.4.2: Motor and Sensory Deficits Associated with Parkinson's Disease:

As mentioned earlier (section 1.2.2.4), output from the basal ganglia is sent to a large number of higher brain centres and possibly also to the MLR. Therefore, it has several possible means by which it might affect the signals sent from the supraspinal centres to the spinal circuitry for locomotion.

It is known that Parkinson's disease results in several motor deficits, including ones associated with gait. The main motor difficulties associated with Parkinson's are a resting tremor, rigidity within the limbs and body, a bradykinesia (slowness of movement), and postural/gait difficulties. There is also a hypokinesia (lack of movement or problem in initiating movements) (Hoehn and Yahr, 1967: Webster, 1968: Delong, 1990). The primary cause of Parkinson's Disease has been determined to be a degeneration of the dopamine producing cells of the substantial nigra. Dopamine is one neurotransmitter used in the Basal Ganglia (as well as throughout the rest of the central nervous system) (Graybiel, 1990).

As well as motor deficits found in Parkinson's disease, investigations have also found deficits in the sensory processing and sensorimotor integration processes within the CNS. A large percentage of Parkinson's patients report sensations such as pain, numbness and tingling that have no apparent cause or relation to the observed motor deficits. Some of these patients have even reported that they felt these strange sensations even before onset of the motor deficits were observed (Koller, 1984). In addition to these sensations, several reports have shown that there is a deficit in the processing of kinesthesic/proprioceptive signals. It has long been observed that people with Parkinson's disease rely more on visual input than those that don't suffer from this disorder. Examination of how well patients perform passive or active movements in the absence of visual input of the moving limb has found that there is a consistent undershooting to the target position (hypometria) (Klockgether, Borutta, Rapp, Speiker, and Dichgans, 1995). In determining which sensory signals were responsible for this undershooting, the kinesthetic monitoring of the position of the arm seemed to be incorrect. When tactile information was provided, either correction was made or the patients commented that they knew that they had undershot the position, something they didn't do if tactile sensation wasn't present (Jobst, Melnick, Byl, Dowling, and Aminoff, 1997). A recent study was done using Positron Emission Topography (PET) to examine changes in brain activity when a sensory stimulus (vibration) is applied to the immobilized metacarpal joint of the index finger in both Parkinsonian patients and matched control subjects. There was significant reduction in Parkinsonian patients compared to control subjects in brain activity related to sensory processing and motor output in the hemisphere contralateral to the side of stimulus application. Specifically, there was reduced activity found in the contralateral primary sensorimotor (M1/S1) and lateral premotor cortex, the contralateral S2, the contralateral posterior cingulate gyrus, the contralateral basal ganglia and bilaterally in the prefrontal cortex (Brodmann area 10). With specific regards to the basal ganglia, vibratory sensory stimulus caused increased activity in the contralateral globus pallidus in control subjects. However, in parkinsonian subjects, no activation of this area, or any area of the basal ganglia, was observed (Boecker, Ceballos-Baumann, Bartenstein, Weindl, Siebner, Fassbender, Munz, Schwaiger and Conrad, 1999). So, it appears that at least part of the motor symptoms that are found with Parkinson's disease arise from problems with sensory and motor processing and the integration of these processes.

1.4.3: Deficits in Parkinsonian Gait:

Several studies have outlined the changes in the gait patterning found in Parkinsonian gait. Knutsson described it as problems resulting from:

> "...varying combinations of hypokinesia, rigidity, as well as defects of posture and equilibrium, and they include the characteristic shuffling gait with small steps, poverty of movements in the trunk and reduced, associated movements of the upper limbs. The initiation of locomotion is difficult and eventually the gait becomes arrested, 'frozen', or an involuntary hastening in gait, propulsion (or festination) may occur. Under strong voluntary effort these deficits may be improved, but when concentration lapses after a short time the usual shuffling, small-stepped gait is resumed."
>
> E. Knutsson, 1972

In examining the temporal parameters of gait, Parkinson's patients generally have a reduced walking speed and stride length. They spent a greater percentage of the step cycle in stance and the double support phase (Knutsson, 1972; Murray, Sepic, Gardner and Downs, 1978; Blin, Ferrandez and Serratrice, 1990). Morris and colleagues found when comparing step velocity, stride length and cadence between Parkinsonian patients and age-matched control subjects, that while stride length was decreased in Parkinson's patients from that seen in the control subjects, their cadence was increased. Also, Parkinson's patients could vary both stride length and cadence when asked to walk at faster or slower speeds in the same linear model as that used by controls, though the range of values they could vary the parameters by was reduced. They also found that while the Parkinson's patients could vary their cadence using both internal motor control mechanisms and external cues, they had difficulty regulating stride length through internal mechanisms, though they could regulate it to external visual cues (Morris, Iansek, Matyas and Summers, 1994). They hypothesized that Parkinson's patients would use increases in cadence to compensate for their difficulty in regulating their stride length, such that a reasonable step velocity could be maintained. A subsequent study showed that Parkinson's patients could regulate their stride length to that of control values either though visual cues or conscious attentional strategies where they visualized how far they should step in their heads. Futhermore, after training with these cues and attentional strategy, they retained the ability to step the control stride length for at least 2 hours, though this retention was lost by the morning after the test session. Furthermore, if a secondary attentional task was given to them to perform while stepping, their stride length (and hence, velocity of stepping) would revert back towards their own baseline values. As well, covert analysis of their gait patterns when the patients were not aware of being tested again showed a reversion to baseline values. It was hypothesized that Parkinson's patients do have the ability to generate a normal walking pattern, but that they rely on attentional processes to modulate their walking. When attention is directed away from the walking task, the gait pattern reverts to the automatic motor program. This program may be faulty due to the fact that lack of basal ganglia input to the motor set may lead to inadequate gain in the mechanisms that cause movement execution, which results in the shortening of successive steps (Morris, Iansek, Matyas and Summers, 1997).

There appears to be some disagreement in terms of step duration, as Knutsson reports a longer step duration in parkinsonian gait, while Murray and her colleagues report no change in the step duration for the patients from the normal controls. The kinematics also differs from that of normal control subjects. The hip joint is not as flexed as in normal controls at the start of the stance phase, while the knee joint is more flexed than normal at the start of stance. There is decreased flexion of the knee during swing phase. The ankle joint does not plantarflex as much in these patients as in normals at both the start and end of the stance phase, leading to a flat-footed, shuffling gait (Knutsson, 1972; Murray et al., 1978). The patients tend to walk with a stooped, flexed posture of the head and neck, with very little arm swing. Their toe clearance is very reduced from normal values during toe swing as well (Murray et al., 1978).

Martin (1967) made an interesting observation when investigating the difficulties Parkinson's patients have in the initiation of the walking cycle. In a group of patients, who couldn't initiate a step cycle by themselves or took very small, shuffling steps, he found that by rocking them from side to side, allowed for them to step almost normally. It appeared that shifting their body weight onto one leg allowed for a normal stepping pattern to become expressed. In normal subjects, it was found that to initiate a step, postural adjustments occur that shift the weight of the body (as measured by the Centre of Mass, or CofM) forward and laterally unto the stance limb (Burleigh, Horak and Malouin, 1994). Parkinsonian patients exhibited decreased force production during push-off, though they spent a longer time in that phase of the step cycle. They also had slowed execution of the required postural adjustments, with smaller excursion of those adjustments, such that movement of the weight of the body onto the stance limb was compromised (Burleigh-Jacobs, Horak, Nutt, and Obeso, 1997). Even in a standing task, where subjects were asked to shift their weight either from side-to-side, or forwards and backwards, Parkinsonian patients showed a much smaller movement amplitude (Beckley, Panzer, Remlet, Ilog and Bloem, 1995). Thus, it appears that these patients may have difficulties in unweighting the swing leg to begin walking. Studies on rats that have had unilateral lesions to the dopamine system showed similar effects in that they would shift their centre of gravity to their "good side" (the one ipsilateral to the lesion, which is unaffected). This is done partly to maintain equilibrium and partly to remove weight from their "bad limbs" so that they could initiate the swing phase of walking. It appears that the rats could also not produce enough force for correcting posture or producing movement with their affected limbs (Miklyaeva, Martens and Whishaw, 1995).

Some evidence shows that patients with Parkinson's Disease show different effects of activation of the group Ib reflex arc from the normal expected inhibitory effects seen in synergistic muscles. Delwaide and colleagues used the condition-test paradigm developed by Pierrot-Deseilligny and colleagues (Pierrot-Deseilligny et al, 1979, Pierrot-Deseilligny et al.,

1983) to examine the effects of a conditioning MG group I stimulus on the soleus H-reflex during relaxed sitting in both Parkinson's patients and normals. The normal subjects showed the inhibition at condition-test intervals indicative of a disynaptic pathway that had been reported previously (Pierrot-Deseilligny et al., 1979; Pierrot-Deseilligny et al, 1983; Chapter 2). The Parkinson's patients, on the other hand, showed no inhibition of the Soleus H-reflex with the conditioning MG afferent stimulation at the disynaptic latencies. Instead, the results pooled across subjects studied showed a possible small facilitation at these condition-test intervals. The results of the Parkinsons patients were significantly different from those of the control subjects (Delwaide, Pepin and Maertens de Noordhout, 1991).

Another study has examined Parkinsonian gait under conditions of decreased body weight in a method similar to that discussed in section 1.1.4. It was found that under normal walking conditions, people with Parkinson's disease showed less extensor thrust and greater flexor activation than that seen in both young adults and normal elderly people. However, they were not able to adjust the activation of the muscles to the same degree that both the other groups were able to under the conditions where decreased loading on the legs was present (Dietz and Colombo, 1998). It was concluded that this decrease in sensitivity to adjust for changes in extensor load is one of the reasons why the patients gait may be impaired.

From these studies, load does seem to play some effect in the gait difficulties found with Parkinson's disease. Also, there have been studies that have shown that group I reflex modulation does change in static conditions with this disorder. It could be possible that this reflex modulation might also be changed from normal during walking, and could contribute to some of the problems found with monitoring the load placed on the extensor muscles during gait. As the response to group I afferent stimulation at disynpatic latencies changed from inhibition to a trend towards facilitation (Delwaide et al., 1991), we hypothesized that this reflex could be modified in the same manner during walking. It may be that the descending input to the locomotor CPG is modified from that found in neurologically normal adults, and as a result, it is processing the afferent input indicating the load or tension from the extensor muscles incorrectly. The final study of this thesis (Chapter 5) was done to examine if there were any changes found in the group I reflex modulation during walking with Parkinson's disease. We again used the paradigm developed by Pierrot-Deseilligny and colleagues (1979), as well as a train of stimuli at slightly below motor threshold levels to the tibial nerve at the level of the popliteal fossa, to activate the group I afferents of the ankle extensors

1.5: Summary of Contents of this Thesis:

As mentioned at the beginning of this chapter, this thesis examines the effect of increased loading on the extensor muscles during human locomotion. The purposes and hypotheses of each of the studies that comprise this thesis are outlined below.

Chapter Two of the thesis investigates whether the effects of group Ib afferent activation is reversed between rest and walking in the intact human nervous system, as it is in reduced animal preparations. The hypothesis is that the inhibitory effects of group Ib afferents at rest would be reversed to a facilitatory influence during walking.

Chapter Three examines the effects of increased and decreased loading during various parts of the stance phase on the magnitudes of activation of various muscles of the lower limb.

As well, timing of the step cycle and its components are looked at to see if a change in duration of any of these phases is seen. The hypothesis was that there would be significant increase in the activation of the extensor muscles of the lower limb with an increase in load on the leg. As well, there would be changes in the timing of the step cycle pattern with changes in load, with an increase in the duration of the stance phase (and resultant increase in step cycle duration) with the increase in load. Opposite effects would be seen with a decrease in load on the leg.

Chapter Four outlines the effect of increased loading on the stepping reflex patterning in young infants. Previous research had indicated that some of the supraspinal connections might not be functionally mature, which would be somewhat analogous to reduced animal preparations. It was hypothesized that there would be changes in the magnitude of activation of the extensor muscles of the limb, as well as changes in the timing of the stepping pattern similar to those seen in reduced animal preparations.

Chapter Five presents the results of the study investigating the effects of activation of group Ib afferents on the Soleus H-reflex and the step cycle durations of walking in Parkinsonian patients. It was hypothesized that the problems found in initiating the swing phase during walking in Parkinsonian gait might be partially due to incorrect processing of the afferent input that registers load to the spinal central pattern generator. As such the CPG still inteprets the leg as being loaded when it is not.

Chapter Six summarizes the results of the above experiments and outlines general conclusions. As well, consideration is given to where the experiments could be improved and where future research could focus.

1.6 REFERENCES:

Alexander G.E. and Crutcher M.D., 1990. Functional architecture of basal ganglia circuits: neural substrates of parallel processing. *TINS 13*(7): 266-271.

Amos A., Armstrong D.M. and Marple-Horvat D.E., 1989. Responses of motor cortical neurones in the cat to unexpected perturbations of locomotion. *Neurosci. Letts. 104*: 147-151.

Andersson O. and Grillner S., 1981. Peripheral control of the cat's step cycle. I. Phase dependent effects of ramp-movements of the hip during "fictive locomotion". *Acta Physiol. Scand. 113*: 89-101..

Andersson O. and Grillner S., 1983. Peripheral control of the cat's step cycle: II. Entrainment of the central pattern generators for locomotion by sinusoidal hip movements during "fictive locomotion." *Acta Physiol. Scand. 118*: 229-239.

Andre-Thomas and Autgarden S., 1966. *Locomotion from pre- to post-natal life: how the newborn begins to acquire psyco-sensory functions. Clinics in Developmental Medicine, No. 24.*

Angel M.J., Guertin P., Jimenez I. and McCrea D.A., 1996. Group I extensor afferents evoke disynaptic EPSPs in cat hindlimb extensor motorneurones during fictive locomotion. *J. Physiol. 494*(3): 851-861.

Armand J., Edgley S.A., Lemon R.N. and Olivier E., 1994. Protracted postnatal development of corticospinal projections from the primary motor cortex to hand motorneurones in the macaque monkey. *Exp. Brain Res. 101*(1): 178-182.

Armstrong D.M. and Drew T., 1984. Discharges of pyramidal tract and other motor cortical neurones during locomotion in the cat. *J. Physiol. 346*: 471-495.

Armstrong D.M. and Drew T., 1985. Forelimb electromyographic responses to motor cortex stimulation during locomotion in the cat. *J. Physiol. 367*: 327-351.

Barker A.T., Freeston I.L., Jalinous R. and Jarratt J.A., 1987. Magnetic stimulation of the human brain and peripheral nervous system: an introduction and the results of an initial clinical evaluation. *Neurosurg. 20*(1): 100-109.

Beckley D.J., Panzer V.P., Remler M.P., Ilog L.B., and Bloem B.R., 1995. Clinical correlates of motor performance during paced postural tasks in Parkinson's disease. *J. Neurological Sci. 132*: 133-138.

Beresovskii V.K. and Bayev K.V., 1988. New locomotor regions of the brainstem revealed by means of electrical stimulation. *Neuroscience 26*(3): 863-869.

Berger W., Horstman G. and Dietz V., 1984. Tension development and muscle activation in the leg during gait in spastic hemiparesis: independence of muscle hypertonia and exaggerated stretch reflexes. *J. Neurology, Neurosurg. Psychiat. 47*: 1029-1033.

Blin O., Ferrandez A.M. and Serratrice G., 1990. Quantitative analysis of gait in Parkinson patients: increased variability of stride length. *J. Neurol. Sci. 98*: 91-97.

Boecker, H., Ceballos-Baumann, A., Bartenstein, P., Weindl, A., Siebner, H.R., Fassbender, T., Munz, F., Schwaiger, M., and Conrad, B., 1999. Sensory processing in Parkinson's and Huntington's disease: Investigations with 3D $H_2{}^{15}O$-PET. *Brain 122*: 1651-1665.

Bouaziz Z., Bouaziz M. and Hugon M., 1975. Modulation of soleus electromyogram during electrical stimulation of medial gastrocnemius nerve in man. *Electromyogr. clin. Neurophysiol. 15*: 31-42.

Brody B.A., Kinney H.C., Kloman A.S. and Gilles F.H., 1987. Sequence of central nervous system myelination in human infancy. I. an autopsy study of myelination. *J. Neuropathology and Exp. Neurol. 46*(3): 283-301.

Bruce I.C. and Tatton W.G., 1980. Synchronous development of motor cortex output to different muscles in the kitten. *Exp. Brain Res. 40*: 349-353.

Bruce I.C. and Tatton W.G., 1981. Descending projections to the cervical spinal cord in the developing kitten. *Neurosci. Letts. 25*(3): 227-231.

Burleigh A.L., Horak F.B. and Malouin F., 1994. Modification of postural responses and step initiation: evidence for goal-directed postural interactions. *J. Neurophysiol. 72*(6): 2892-2902.

Burleigh-Jacobs A.L., Horak F.B., Nutt J.G. and Obeso J.A., 1997. Step initiation in Parkinson's disease: influence of levadopa and external sensory triggers. *Movement Disorders 12*(2): 206-215.

Buschges A. and El Manira A., 1998. Sensory pathways and their modulation in the control of locomotion. *Current Opinion in Neurobiology 8*: 733-739.

Calancie B., Needham-Shropshire B., Jacobs P., Willer K., Zych G. and Green B.A., 1994. Involuntary stepping after chronic spinal cord injury: evidence for a central rhythm generator for locomotion in man. *Brain 117*: 1143-1159.

Capaday C., Lavoie B.A., Barbeau H., Schneider C. and Bonnard M., 1999. Studies on the corticospinal control of human walking: I. Responses to focal transmagnetic stimulation of the motor cortex. *J. Neurophysiol. 81*: 129-139.

Choa B.H.G. and Stephens J.A., 1982. Cutaneous reflex responses and central nervous lesions studied in the lower limb in man. *J. Physiol. 328*: 23P-24P

Clarac F., Vinay L., Cazalets J.R., Fady J.C. and Jaman M., 1998. Role of gravity in development of posture and locomotion in the neonatal rat. *Brain Res. Brain Res. Reviews 28*(1-2): 35-43.

Coles S.K., Iles J.F., Nicolopoulos-Stournaras S., 1989. The mesencephalic centre controlling locomotion in the rat. *Neuroscience 28*(1): 149-157.

Conway B.A., Hultborn H. and Kiehn O., 1987. Proprioceptive input resets central locomotor rhythm in the spinal cat. *Exp. Brain Res. 68*: 643-656.

Crum J.E. and Stephens J.A., 1982. Cutaneous reflex responses recorded in the lower limb of the newborn infant. *J. Physiol. 332*: 30P-31P.

Delong M.R., 1990. Primate models of movement disorders of basal ganglia origin. *TINS 13*(7): 281-285.

Delwaide P.J., Pepin J.L. and Maertens de Noordhout A., 1991. Short-latency autogenic inhibition in patients with parkinsonian rigidity. *Ann. Neurol. 30*: 83-89

Dietz V. and Colombo G., 1998. Influence of body load on the gait pattern in Parkinson's disease. *Movement Disorders 13*(2): 255-261.

Dietz V., Colombo G. and Jensen L., 1994. Locomotor activity in spinal man. *Lancet 344*: 1260-1263.

Dimitrijevic M.R., Gerasimenko Y. and Pinter M.M., 1998. Evidence for a spinal central pattern generator in humans. In: *Neuronal Mechanisms for Generating Locomotor Activity, Annals of the New York Academy of Sciences, Vol. 860.* (eds.) Kiehn O., Harris-Warrick R.M., Jordan L., Hultborn H. and Kudo N., New York, pp 360-376.

Donelan J.M., and Kram R., 1997). The effect of reduced gravity on the kinematics of human walking: a test of the dynamic similarity hypothesis for locomotion. *J. Dev. Biol. 200*: 3193-3201.

Drew T., 1988. Motor cortical cell discharge during voluntary gait modification. *Brain Res. 457*: 181-187.

Durelli L., Schmidt E.M., McIntosh J.S., and Bak M.J., 1978. Single-unit chronic recordings from the sensorimotor cortex of unrestrained cats during locomotion. *Exp. Neurol. 62*(3): 580-594.

Duysens J., 1977. Reflex control of locomotion as revealed by stimulation of cutaneous afferents in spontaneously walking premammillary cats. *J. Neurophysiol. 40*(4): 737-751.

Duysens J., Clarac F., and Cruse H., 2000. Load-regulating mechanisms in gait and posture: comparative aspects. *Physiological Reviews 80*(1): 83-133.

Duysens J. and Pearson K.G., 1976. The role of cutaneous afferents from the distal hindlimb in the regulation of the step cycle of thalamic cats. *Exp. Brain Res. 24*: 245-255.

Duysens J. and Pearson K.G., 1980. Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Res. 187*: 321-332.

Eccles J.C., Eccles R.M. and Lundberg A., 1957. Synaptic actions on motorneurones by impulses in Golgi tendon organ afferents. *J. Physiol. 138*: 227-252.

Eke-Okoro S.T. and Larsson L.-E., 1984. A comparison of the gaits of paretic patients with the gaits of control subjects carrying a load. *Scand. J. Rehab. Med. 16*: 151-158.

Eyre J.A., Miller S. and Ramesh V., 1991. Constancy of central conduction delays during development in man: investigation of motor and somatosensory pathways. *J. Physiol. 434*: 441-452.

Finch L., Barbeau H. and Arsenault B., 1991. Influence of body weight support on normal human gait: development of a gait retraining strategy. *Physical Therapy 71*(11):842-856.

Flament D., Goldsmith P. and Lemon R.N., 1992. The development of corticospinal projections to tail and hindlimb motorneurons studied in infant macaques using magnetic brain stimulation. *Exp. Brain Res. 90*(1): 225-228.

Flament D., Hall E.J. and Lemon R.N., 1992. The development of cortico-motorneuronal projections investigated using magnetic brain stimulation in the infant macaque. *J. Physiol. 447*: 755-768.

Forssberg H., 1982. Spinal locomotor functions and descending control. In: *Brain Stem Control of Spinal Mechanisms.* (eds.) B. Sjolund and A. Bjorklund. Elsevier Biomedical Press. pp. 253-271.

Forssberg H., 1985. Ontogeny of human locomotor control. I. infant stepping, supported locomotion and transition to independent locomotion. *Exp. Brain Res. 57*: 480-493.

Forssberg H., Grillner S. and Rossignol S., 1975. Phase dependent reflex reversal during walking in chronic spinal cats. *Brain Res. 85*(1): 103-107.

Forssberg H., Grillner S. and Rossignol S., 1977. Phasic gain control of reflexes from the dorsum of the paw during spinal locomotion. *Brain Res. 132*(1): 121-139.

Forssberg H. and Wallberg H., 1980. Infant locomotion: a preliminary movement and electromyographic study. In: *Children and Exercise IX: One series in sports sciences, Volume 10.* (eds) K. Berg and B.O. Eriksson. University Park Press, Baltimore, Maryland. pp.32-40.

Fouad K. and Pearson K.G., 1997. Effects of extensor muscle afferents on the timing of locomotor activity during walking in adult rats. *Brain Res. 749*(2): 320-328.

Fung J. and Barbeau H., 1994. Effects of conditioning cutaneomuscular stimulation on the soleus H-reflex in normal and spastic paretic subjects during walking and standing. *J. Neurophysiol. 72*(5): 2090-2104.

Garcia-Rill E. and Skinner R.D., 1987a. The mesencephalic locomotor region. I. Activation of a medullary projection site. *Brain Res. 411*: 1-12.

Garcia-Rill E. and Skinner R.D., 1987b. The mesencephalic locomotor region. II. Projections to reticulospinal neurons. *Brain Res. 411*: 13-20.

Garcia-Rill E., Skinner R.D. and Gillmore S.A., 1981. Pallidal projections to the mesencephalic locomotor region (MLR) in the cat. *Amer. J. of Anat. 161*, 311-321.

Garcia-Rill E., Skinner R.D., Jackson M.B. and Smith M.M., 1983. Connections of the mesencephalic locomotor region (MLR) I. substantia nigra afferents. *Brain Res. Bull. 10*(1): 57-62.

Ghori G.M.U. and Luckwill R.G., 1985. Responses of the lower limb to load carrying in walking man. *Eur. J. Appl. Physiol. 54*: 145-150.

Gorassini M.A., Prochazka A., Hiebert G.W. and Gaultier M.J.A., 1994. Corrective responses to loss of ground support during walking. I. intact cats. *J. Neurophysiol. 71*(2): 603-610.

Goslow G.E., Reinking R.M. and Stuart D., 1973. The cat step cycle: hind limb joint angles and muscle lengths during unrestrained locomotion. *J. Morphol. 141*: 1-41.

Gossard J-P., Brownstone R.M., Barajon I. and Hultborn H., 1994. Transmission in a locomotor-related group Ib pathway from hindlimb extensor muscles in the cat. *Exp. Brain Res. 48*(2): 213-228.

Graybiel A.M., 1990. Neurotransmitters and neuromodulators in the basal ganglia. *TINS 13*(7): 244-254.

Grillner S., 1981. Control of locomotion in bipeds, tetrapods and fish. In: *Handbook of Physiology, Sect. 1: The Nervous System, Vol. II: Motor Control,* Part 2 (ed.) Brooks V.B.. American Physiological Society, Bethesda. pp. 1179-1236.

Grillner S. and Debuc R., 1988. Control of locomotion in vertebrates: spinal and supraspinal mechanisms. In: *Advances in Neurology. Vol. 47. Functional Recovery in Neurological Disease.* (ed). S.G. Waxman. Raven Press. New York. pp. 425-453.

Grillner S. and Rossignol S., 1978. On the initiation of the swing phase of locomotion in chronic spinal cats. *Brain Res. 146*: 269-277.

Grillner S. and Wallen P., 1985. Central pattern generators for locomotion, with special reference to vertebrates. *Ann. Rev. Neurosci. 8*: 233-261.

Grillner S. and Zangger P., 1975. How detailed is the central pattern generation for locomotion? *Brain Res. 88*(2): 367-371.

Grillner S. and Zangger P., 1979. On the central generation of locomotion in the low spinal cat. *Exp. Brain Res. 34*(2): 241-261.

Grote J.R., 1981. The effect of load on locomotion in crayfish. *J. Exp. Biol. 92*: 277-288.

Guertin P., Angel M.J., Perreault M.-C. and McCrea D.A., 1995. Ankle extensor group I afferents excite extensors throughout the hindlimb during fictive locomotion in the cat. *J. Physiol. 487*(1): 197-209.

Hanakawa T., Katsumi Y., Fukuyama H., Honda M., Hayashi T., Kimura J. and Shibasaki H., 1999. Mechanisms underlying gait disturbance in Parkinson's disease: a single photon emission computed tomography study. *Brain 122*: 1271-1282.

Hanna J.P. and Frank J.I., 1995. Automatic stepping in the pontomedullary stage of central herniation. *Neurology 45*: 985-986.

Harkema S.J., Hurley S.L., Patel U.K., Requejo P.S., Dobkin B.H. and Edgerton, V.R., 1997. Human lumbosacral spinal cord interprets loading during stepping. *J. Neurophysiol. 77*: 797-811.

Hayes, K.C., 1982. Biomechanics of postural control. In: *Exercise and Sport Science Reviews.* (ed.) B.L. Terjury. Franklin Institute Press, Philadelphia, Pennsylvania. pp. 363-391.

Hiebert G.W., Gorassini M.A., Jiang W., Prochazka A. and Pearson K.G., 1994. Corrective responses to loss of ground support during walking. II. comparison of intact and chronic spinal cats. *J. Neurophysiol. 71*(2): 611-622.

Hiebert G.W., Whelan P.J., Prochazka A. and Pearson K.G., 1995. Suppression of the corrective response to loss of ground support by stimulation of extensor group I afferents. *J. Neurophysiol. 73*(1): 416-420.

Hiebert G.W., Whelan P.J., Prochazka A. and Pearson K.G., 1996. Contribution of hind limb flexor muscles afferents to the timing of phase transitions in the cat step cycle. *J. Neurophysiol. 75*(3): 1126-1137.

Hoehn M.M and Yahr M.D., 1967. Parkinsonism: onset, progression, and mortality. *Neurology 17*(5): 427-442.

Hongo T., Lundberg A., Phillips C.G. and Thompson R.F., 1984. The pattern of monosynaptic Ia-connections to hindlimb motor nuclei in the baboon: a comparison with the cat. *Proc. R. Soc. Lond. B. 221*: 261-289.

Humphrey, 1960. The development of the pyramidal tracts in human fetuses, correlated with cortical differentiation. In: *Structure and Function of the Cerebral Cortex.* Tower D.B. and Schade J.P. (eds.), Elsevier, Amsterdam. pp. 93-103.

Issler H. and Stephens J.A., 1983. The maturation of cutaneous reflexes studied in the upper limb in man. *J. Physiol. 335*: 643-654.

Jobst E.E., Melnick, M.E., Byl N.N., Dowling G.A. and Aminoff M.J., 1997. Sensory perception in Parkinson disease. *Arch. Neurol. 54*: 450-454.

Jones C.A. and Yang J.F., 1994. Reflex behavior during walking in incomplete spinal-cord-injured subjects. *Exp. Neurol. 128*: 239-248.

Kanda K. and Sato H., 1983. Reflex responses of human thigh muscles to non-noxious sural stimulation during stepping. *Brain Res. 288*(1-2): 378-380.

Klockgether T., Borutta M., Rapp H., Speiker S., and Dichgans J., 1995. A defect of kinesthesia in Parkinson's disease. *Movement Disorders 10*(4): 460-465.

Knutsson E., 1972. An analysis of parkinsonian gait. *Brain 95*: 475-486.

Koh T.H. and Eyre J.A., 1988. Maturation of corticospinal tracts assessed by electromagnetic stimulation of the motor cortex. *Arch. Of Disease in Children 63*(11): 1347-1352.

Koller, W.C., 1984. Sensory symptoms in Parkinson's disease. *Neurology 34*: 957-959.

Kriellaars D.J., Brownstone R.M., Noga B.R. and Jordan L.M., 1994. Mechanical entrainment of fictive locomotion in the decerebrate cat. *J. Neurophysiol. 71*(6): 2074-2086.

Kuypers H.G.J.M., 1962. Corticospinal connections: postnatal development in the rhesus monkey. *Science 138*: 678-680.

Laporte Y. and Lloyd D.P.C., 1952. Nature and significance of the reflex connections established by large afferent fibres of muscular origin. *Am. J. Physiol. 169*: 609-621.

Mao C.C., Ashby P., Wang M. and McCrea D.A., 1984. Synaptic connections from large muscle afferents to the motorneurons of various leg muscles in man. *Exp. Brain Res. 56*: 341-350.

Martin J.P., 1967. Locomotion and the basal ganglia. In: *The Basal Ganglia and Posture.* Pitman Medical Publishing Co. Ltd. London. pp.20-35.

Masdeu J.C., Alampur U., Cavaliere R., and Tavoulareas G., 1994. Atasia and gait failure with damage of the pontomesencephalic locomotor region. *Ann. Neurol. 35*(5): 619-621.

Mayer R.F. and Mosser R.S., 1969. Excitability of motorneurons in infants. *Neurology 19*: 932-945.

Mayson M.J., Harrison L.M., Quinton R., Stephens J.A., Krams M. and Bouloux P.-M. B., 1997. Mirror movements in X-linked Kallmann's syndrome. I. a neurophysiological study. *Brain 120*: 1199-1216.

McCraw M.B., 1940. Neuromuscular development of the human infant as exemplified in the achievement of erect locomotion. *J. Pediatr. 17*: 747-777.

McCrea D.A., Shefchyk S.J., Stephens M.J. and PearsonK.G., 1995. Disynaptic group I excitation of synergist ankle extensor motorneurons during fictive locomotion in the cat. *J. Physiol. 487*: 527-539.

Miklyaeva E.I., Martens D.J., and Whishaw I.Q., 1995. Impairments and compensatory adjustments in spontaneous movement after unilateral dopamine depletion in rats. *Brain Res. 681*: 23-40.

Mori S., Matsui T., Kuze B., Asanome M., Nakajima K. and Matsuyama K., 1999. Stimulation of a restricted region in the midline cerebellar white matter evokes coordinated quadrupedal locomotion in the decerebrate cat. *J. Neurophysiol. 82*: 290-300.

Mori S., Sakamoto T., Ohta Y., Takakusaki K. and Matsuyama K., 1989. Site-specific postural and locomotor changes evoked in awake, freely moving intact cats by stimulating the brainstem. *Brain Res. 505*: 66-74.

Morris M.E., Iansek R., Matyas T.A. and Summers J.J., 1994. The pathogenesis of gait hypokinesia in Parkinson's disease. *Brain 117*: 1169-1181.

Morris M.E., Iansek R., Matyas T.A. and Summers J.J., 1996. Stride length regulation in Parkinson's disease: Normalization strategies and underlying mechanisms. *Brain 119*: 551-568.

Muller K., Homberg V. and Lenard H.C., 1991. Magnetic stimulation of motor cortex and nerve roots in children. Maturation of cortico-motorneuronal projections. *Electroencephalography and Clin. Neurophysiol. 81*(1): 63-70.

Murray M.P., Seireg A.A., and Sepic S.B., 1975. Normal postural stability and steadiness: quantitative assessment. *J. Bone and Joint Surgery 57A*(4): 510-516.

Murray M.P., Sepic S.B., Gardner G.M. and Downs W.J., 1978. Walking patterns in men with parkinsonism. *American Journal of Physical Medicine 57*(6): 278-294.

Neumann D.A. and Cooke T.M., 1985. Effect of load and carrying position on the electromyographic activity of the gluteus medius muscle during walking. *Physical Therapy 65*(3): 305-311.

Nezu A., Kimura S., Uehara S., Kobayashi T., Tanaka M. and Saito K., 1997. Magnetic stimulation of motor cortex in children: maturity of corticospinal pathway and problem of clinical application. *Brain and Development 19*(3): 176-180.

Nilsson J., Thorstensson, A., and Halbertsma, J., 1985. Changes in leg movements and muscle activity with speed of locomotion and mode of progression in humans. *Acta Physiol. Scand. 123*: 457-475.

Okamoto, T., and Gott Y., 1985. Human infant pre-independent and independent walking. In: *Primate Morphophysiology, locomotor analyses and human bipedalism,* pp. 25-45, University of Tokyo Press, Tokyo.

Orlovsky G.N., 1970a. Influence of the cerebellum on the reticulospinal neurones during locomotion. *Biophysics 15*: 928-936.

Orlovsky G.N., 1970b. Work of the reticulo-spinal neurones during locomotion. *Biophysics 15*: 761-771.

Orlovsky G.N., 1972. Work of the neurones of the cerebellar nuclei during locomotion. *Biophysics 17*: 1177-1185.

Pearson K.G., 1976. The control of walking. *Sci. Amer. 235*: 72-86.

Pearson K.G., 1993. Common principles of motor control in vertebrates and invertebrates. *Annu. Rev. Neurosci. 16*: 265-297.

Pearson K.G. and Collins D.F., 1993. Reversal of the influence of group Ib afferents from plantaris on activity in medial gastrocnemius muscle during locomotor activity. *J. Neurophysiol. 70*(3): 1009-1017.

Pearson K.G., Ramirez J.M. and Jiang W., 1992. Entrainment of the locomotor rhythm by group Ib afferents from ankle extensor muscles in spinal cats. *Exp. Brain Res. 90*: 557-566.

Perreault M-C., Angel M.J., Guertin P., and McCrea D.A., 1995. Effects of stimulation of hindlimb flexor group II afferents during fictive locomotion in the cat. *J. Physiol. 487*(pt. 1): 211-220.

Perreault M-C., Enriquez-Denton M., and Hultborn H., 1999. Proprioceptive control of extensor activity during fictive scratching and weight support compared to fictive locomotion. *J. Neurosci. 19*(24): 10966-10976.

Pierrot-Deseilligny E., Bergego C., and Mazieres L., 1983. Reflex control of bipedal gait in man. In: *Motor Control Mechanisms in Health and Disease,* (ed.) Desmedt, J.E. Raven Press, New York. pp. 699-716.

Pierrot-Deseilligny E., Katz R. and Morin C., 1979. Evidence for Ib inhibition in human subjects. *Brain Res. 166*: 176-179.

Pierrot-Deseilligny E., Morin, C., Bergego, C. and Tankov, N., 1981. Pattern of group I fibre projections from ankle flexor and extensor muscles in man. *Exp. Brain Res. 42*: 337-350.

Pratt C.A., 1995. Evidence of positive force feedback among hindlimb extensors in the intact standing cat. *J. Neurophysiol. 73*(6): 2578-2583.

Rossignol S., Lund J.P. and Drew T., 1988. The role of sensory inputs in regulating patterns of rhythmical movements in higher vertebrates: a comparison between locomotion, respiration and mastication. In: *Neural Control of Rhythmic Movements in Vertebrates.* (eds) A. Cohen, S. Rossignol and S. Grillner. John Wiley and Sons Inc., New York. pp. 201-283.

Rowlandson P.H. and Stephens J.A., 1985a. Maturation of cutaneous reflex responses recorded in the lower limb in man. *Dev. Med. Child Neurol. 27*(4): 425-433.

Rowlandson P.H. and Stephens J.A., 1985b. Cutaneous reflex responses recorded in children with various neurological disorders. *Dev. Med. Child Neurol. 27*(4): 434-447.

Schreyer D.J. and Jones E.G., 1982. Growth and target finding by axons of the corticospinal tract in prenatal and postnatal rats. *Neuroscience 7*(8): 1837-1853.

Schomberg E.D., Petersen N., Barajon I. and Hultborn H., 1998. Flexor reflex afferents reset the step cycle during fictive locomotion in the cat. *Exp. Brain Res. 122*: 339-350.

Shik M.L., Severin F.V. and Orlovsky G.N., 1966. Control of walking and running by means of stimulation of the mid-brain. *Biophysics 11*: 756-765.

Sinkjaer T., Toft E. and Hansen H.J., 1995. H-reflex modulation during gait in multiple sclerosis patients with spasticity. *Acta Neurol. Scand. 91*: 239-246.

Stein R.B., Yang J.F., Belanger M. and Pearson K.G., 1993. Modification of reflexes in normal and abnormal movements. In: *Progress in Brain Research: Vol. 97.* (eds.) J.H.J. Allum, D.J. Allum-Mecklenburg, F.P. Harris and R. Probst. Elsevier Science Publishers B.V. pp. 189-196.

Thelen E. and Cooke D.W., 1987. Relationship between newborn stepping and later walking: a new interpretation. *Dev. Med. and Child Neurol. 29*: 380-393.

Thomas J.E. and Lambert E.H., 1960. Ulnar nerve conduction velocity and H-reflex in infants and children. *J. Appl. Physiol. 15*(1): 1-9.

Vilensky, J.A., 1987. Locomotor behavior and control in human and non-human primates: Comparisons wiht cats and dogs. *Neurosci. and Behavioral Reviews 11*:263-274.

Websfer D.D., 1968. Critical analysis of the disability in Parkinson's disease. *Modern Treatment 5*(2): 257-282.

Wentik G.H., 1976. The action of the hind limb musculature of the dog in walking. *Acta Anat. 96*: 70-80.

Whelan P.J., Hiebert G.W. and Pearson K.G., 1995. Stimulation of the group I extensor afferents prolongs the stance phase in walking cats. *Exp. Brain Res. 103*: 20-30.

Whelan P.J. and Pearson K.G., 1997. Comparison of the effects of stimulating extensor group I afferents on cycle period during walking in conscious and decerebrate cats. *Exp. Brain Res. 117*: 444-452.

Yakolev P.I. and Lecours A-R., 1967. The myelogenetic cycles of regional maturation of the brain. In: *Regional Development of the Brain in Early Life*. (ed.) A Minkowski. Oxford, UK: Blackwell. pp. 3-70.

Yang J.F., Fung J., Edamura M., Blunt R., Stein R.B. and Barbeau H., 1991. H-reflex modulation during walking in spastic paretic subjects. *Can. J. Neurological Sciences 18*(4): 443-452.

Yang J.F. and Stein R.B., 1990. Phase-dependent reflex reversal in human leg muscles during walking. *J. Neurophysiol. 63*(5): 1109-1117.

Yang J.F., Stephens M.J and Vishram R., 1998. Infant stepping: a method to study the sensory control human stepping. *J. Physiol. (Lond.) 507*: 927-937.

Zelazo P.R., Zelazo N.A. and Kolb S., 1972. "Walking" in the newborn. *Science 176*: 314-315.

2.0 SHORT LATENCY, NON-RECIPROCAL GROUP I INHIBITION IS REDUCED DURING THE STANCE PHASE OF WALKING IN HUMANS*

2.1 INTRODUCTION

The processing of sensory information is dependent on the movement task an animal or person is engaged in (reviewed in Stein and Capaday, 1987). Load sensitive responses are a good example of how this sensory processing changes. When the animal is quiet, loading of a limb activates receptors to oppose the disturbance by providing negative feedback to the appropriate muscles. During movement, however, the same receptors provide positive feedback to assist the movement. This phenomenon has been observed in animals as diverse as insects (Bassler, 1976), arthropods (Skorupski and Sillar, 1986) and mammals (Duysens and Pearson, 1980).

In the cat, for example, activation of group Ib afferents from the force sensitive Golgi tendon organs inhibit the homonymous and synergistic muscles and excite the antagonistic muscles under resting conditions (Eccles, Eccles and Lundberg, 1957; Laporte and Lloyd, 1952). During locomotion, on the other hand, the force generated in the extensor muscles enhances extensor activity (Duysens and Pearson, 1980). This type of reflex-reversal has been reported for immobilized spinal (Conway, Hultborn, and Kiehn, 1987; Gossard, Brownstone, Barajon, and Hultborn, 1994), non-immobilized spinal (Pearson and Collins, 1993), immobilized decerebrate (Gossard et al, 1994; McCrea, Shekchyk, Stephens, and Pearson, 1995) and non-immobilized decerebrate (Duysens and Pearson, 1980) cat preparations. There is both a short and long latency component to the excitatory responses seen during walking. The classical disynaptic inhibition seen at rest is greatly reduced in spinal cats and reversed to excitation in decerebrate cats (McCrea et al, 1995). This short latency effect is particularly evident during the extension phase of the step cycle. A longer latency (10 - 40 ms in the cat), slowly rising excitatory effect is seen in both spinal and decerebrate preparations during locomotion (Gossard et al, 1994; Guertin, Angel, Jimenez and McCrea, 1994; Pearson and Collins, 1993). This longer latency effect is particularly strong during the flexor phase of locomotion (McCrea et al, 1995).

---

* This chapter has been published in: Stephens, M.J. and Yang, J.F. (1996). Short latency, non-reciprocal group I inhibition is reduced during the stance phase of walking in humans. Brain Research 743: 24-31. Contribution to paper: Involved with initial pilot testing, recruitment of subjects, development of the protocol for use in walking, data collection, data analysis, statistical analysis, drawing of figures and initial draft of the paper.

The reflex-reversal of load sensitive receptors, as described above, may be very important for walking, particularly for signalling the transition from the stance to the swing phase (Duysens and Pearson, 1980). Functionally, if the load on the extensor muscles remains high, it must indicate that the limb is not ready for the swing phase. If this reflex-reversal is indeed functionally important in this way, it should be especially important for bipeds. With only two limbs to support the weight of the body, proper weight transfer from one limb to the next is essential for safe forward locomotion. Whether this type of reflex-reversal occurs in the bipedal human is unknown.

A putative group Ib reflex is accessible for study in the lower limb of primates. A short latency inhibitory effect is seen in the soleus muscle when the nerve to the medial gastrocnemius (MG) muscle is stimulated at group I strength in non-human primates, and has been attributed to Ib afferents (Hongo, Lundberg, Phillips, and Thompson, 1984). Similar types of responses have been reported in the human. The soleus electromyographic (EMG) activity was depressed when the MG nerve was electrically stimulated (Bouaziz, Bouaziz, and Hugon, 1975; Mao, Ashby, Wang, and McCrea, 1984). This inhibition was also seen when the soleus H-reflex was conditioned by a preceding stimulus to the MG nerve at condition-test intervals that would be appropriate for a disynaptic pathway (Pierrot-Deseilligny, Katz, and Morin, 1979).

The present study determined whether the disynaptic, Ib reflex-reversal demonstrated in cats also occurs in the human. The results indicate that the disynaptic inhibition, seen under resting conditions, is reduced or eliminated during the stance phase of walking, consistent with the results from other animals. Preliminary results have been reported (Stephens and Yang, 1994).

2.2 MATERIALS AND METHODS

The methods used in the present study were originally described by Pierrot-Deseilligny and colleagues (Pierrot-Deseilligny et al, 1979; Pierrot-Deseilligny, Morin, Bergego, and Tankov, 1981). The magnitude of the soleus H-reflex when preceded by a stimulus to the MG nerve was used to assess the strength of a group Ib reflex from the MG muscle to the soleus muscle. The interval by which the stimulus to the MG nerve preceded the stimulus to the tibial nerve was varied to study disynaptic and polysynaptic effects. The strength of the Ib response was studied under 4 conditions: 1) quiet sitting, 2) activating the triceps surae muscle isometrically in sitting at a submaximal level, 3) activating the triceps surae to the same level as 2) during standing, and 4) walking.

Subjects

A total of 16 subjects were studied after obtaining informed, written consent. Not all subjects could be studied under all the conditions, because the procedures necessary to study each of these conditions were lengthy. Twelve subjects were studied initially under two conditions: quiet sitting and walking. Seven of these subjects returned on another day in order to examine the reflex under the two sitting conditions (i.e., conditions 1 and 2 in the above paragraph). In addition, 3 subjects were studied under all three conditions on the same day, but at fewer condition-test intervals. Five subjects were studied under conditions 2 and 3 on another occasion.

Recording Procedures

The H-reflex was recorded from the soleus muscle using bipolar Ag/AgCl surface electrodes (1 cm in diameter) placed approximately one centimetre apart, below the insertion of the gastrocnemius muscle into the Achilles tendon. Another set of surface electrodes was used to monitor the direct motor response (M-wave) from the MG muscle. These electrodes were placed over the portion of the MG muscle that showed contraction at minimum stimulus intensity. The recordings from the soleus and MG muscles were amplified and bandpass filtered (10-1000 Hz). Footswitches were placed under the heel and the ball of the foot to monitor foot-floor contact during walking. The signals were A/D converted (at 2800 Hz) and averaged on-line. The data were also recorded on VHS videotape, using an A/D VCR adapter (Model PCM 4/8, Medical Systems Corp.).

Stimulation Procedures

The soleus H-reflex was elicited by single 1 ms pulses to the tibial nerve at the popliteal fossa with surface electrodes (Beckman type). The anode, a large 2"x2" self-adhesive electrode (Chattanooga Corp.), was placed on the anterior surface of the thigh, just proximal to the patella (see Hugon, 1973). The strength of the stimulus was adjusted to generate a control H-reflex with an amplitude of 10-15% that of the maximum M-wave recorded in quiet sitting. Trials in which the H-reflex fell outside of this range were excluded. The size of the control H-reflex was carefully matched for all tasks, since the susceptibility of the H-reflex to excitation and inhibition is dependent on its size (Crone, Hultborn, Mazieres, Morin, Nielsen, and Pierrot-Deseilligny, 1990; Meinck, 1980). The size of the maximum M-wave was monitored during pilot work and found not to change substantially across the different movement conditions studied (less than 15%).

The MG nerve was stimulated at a site where visible contraction of the MG muscle alone could be seen. This was usually 7 to 10 cm distal and medial to the location of the cathode for the tibial nerve. The stimulus anode for the MG nerve was placed over the anterolateral portion of the leg, just distal to the patella. The stimulus to the MG nerve was 1 ms in duration. Either a single or multiple pulses to the MG nerve was used to condition the soleus H-reflex. When multiple pulses were used, the interpulse interval was 5 ms. Multiple conditioning pulses have been shown to be more effective in generating the short latency inhibition in humans (Bouaziz et al, 1975; Pierrot-Deseilligny et al, 1979). They were also more effective in generating excitatory post-synaptic potentials in motorneurons during walking in the cat (Gossard et al, 1994; McCrea et al, 1995). The number of MG stimuli used in each subject was the minimum number necessary to generate an inhibition at rest (up to a maximum of 4). For example, a trial was done with one pulse of conditioning MG afferent stimulation at a disynaptic interval, usually 6 ms, and the ratio of the condition to control H-reflexes calculated. If no inhibition was found, the number of conditioning pulses was increased to two and the trial repeated. This procedure would be repeated up until 4 pulses of conditioning MG nerve stimulation was used. The final stimulus to the MG nerve preceded the stimulus to the tibial nerve by a condition-test interval that ranged from 1 to 16 ms. The long condition-test intervals were included to determine whether the long latency effects seen in the cat were also observed in the human.

The magnitude of the MG stimulus was kept just below the level which would generate an M-wave in the MG muscle, to ensure that the effects observed were not contaminated by Renshaw inhibition. The motor threshold was checked repeatedly throughout the experiment, to ensure that the stimulus intensity was just subthreshold. In quiet sitting, this is easily done by observing the effect of stimulation on the EMG from the MG muscle on an oscilloscope. During isometric contractions and walking, the effect of stimulation on the MG EMG was averaged on-line, in order to average out the background EMG, thus revealing the M-wave.

The effective strength of the MG stimulus could not be verified during the experimental trials, because of the necessity to keep the MG stimulus below motor threshold. While the effective strength of the stimulus is unlikely to change much under isometric conditions, in walking, this may be a problem. Thus, in pilot work, the effective MG stimulus strength was examined by stimulating the MG nerve at 2 times motor threshold and observing the change in the M-wave recorded from the MG muscle in separate trials. The M-wave varied the least during the middle of the stance phase. Moreover, when the stimulus was triggered at a fixed delay from the time of heel-contact, the variability was less than 15%. Hence, this was the method used in walking.

It was unlikely that the MG stimulus was spreading to the tibial nerve, because the stimulus strength needed to generate an H-reflex in the soleus muscle was more than 4 times greater than the stimulus magnitude needed to generate the M-wave in the MG muscle in most subjects (one subject showed spread at more than 2 times motor threshold, while 3 others showed spread at more than 3 times motor threshold). Similar results have been reported by others (Delwaide and Oliver, 1988; Pierrot-Deseilligny et al, 1981). The stimulus intensity required to generate an H-reflex in the soleus muscle from stimulation of the MG nerve was checked just before collecting data for each task.

General Protocol

In quiet sitting, the subjects sat comfortably with their ankles supported at a 90° angle. Stimuli were applied at regular intervals every 3 seconds in order to minimize the variability associated with the recovery of the H-reflex (Taborikova and Sax, 1969). Three second intervals for successive trials have been used by many others (Crone et al, 1990; Pierrot-Deseilligny et al, 1979). We felt the interval was a reasonable compromise between allowing some recovery of the H-reflex, but not so long as to prolong the experiments excessively.

Control and conditioned H-reflexes were presented alternately, in sequences of 40. Pilot work from 3 subjects showed that when the conditioned H-reflexes were elicited in a group (groups of 20), the degree of inhibition generated was larger than when the conditioned reflexes were alternated with control reflexes. Hence, there seemed to be a slow, cumulative effect of the inhibition when the reflexes were elicited in succession. For this reason, control and conditioned reflexes were presented alternately, as we were only interested in the short latency effects.

For walking, the speed of the treadmill was adjusted to be at a comfortable walking pace for the subject (between 0.9 and 1 m/s). Stimuli were presented every other step during walking, so that the interstimulus interval was close to the 3 s interval used in sitting. The stimuli were triggered after a fixed delay from heel contact so that it arrived in the middle of the stance phase. At this point in the stance phase, the ankle is at 90°, similar to the ankle position in the static trials. The control and conditioned H-reflexes were presented alternately in groups of 80. More responses were averaged for walking, because the variability of the H-reflex was higher.

The effect of a background contraction in the triceps surae muscle group was tested in 9 subjects in sitting. The subjects sat in the same position as that used for the quiet condition, and held a submaximal isometric contraction of the triceps surae group, at a level of approximately 20% maximum. Stronger contractions were found to be too fatiguing for the duration of the experiment. Subjects were given visual feedback of the rectified and filtered EMG to control the level of the contraction.

The effect of standing was tested in 5 subjects on another occasion. The subjects repeated the condition of holding a low level, isometric contraction of 20% maximum in sitting, and then the same level of contraction was repeated in standing. This condition allowed us to determine whether the standing position could account for the changes seen in walking.

Statistical tests

A t-test was used to determine the effect of the conditioning stimulus on the soleus H-reflex during: 1) quiet sitting and 2) walking. Those subjects that showed a significant inhibition ($p<0.1$) during quiet sitting were grouped together for subsequent analyses. A somewhat more liberal level of significance ($p<0.1$) was used here in order to ensure that subjects who showed inhibition were not missed. We feel this is justified, because of the modest levels of inhibition normally seen (e.g., see Gritti and Schieppati, 1989). The conditioned H-reflexes were then expressed as a percentage of the control H-reflex. Two-way repeated measures ANOVA's were also used to compare the results for: 1) walking versus resting, 2) isometric contraction versus resting and 3) isometric contraction during sitting versus during standing. Significant interactions were further analyzed to determine which simple effects were different (Keppel, 1982). The

ANOVA and post-hoc tests were performed at the 95% confidence level.

2.3 RESULTS

Inhibition of the soleus H-reflex in sitting

An example of the control and conditioned soleus H-reflex from a single subject during quiet sitting is shown for the condition-test interval of 5 ms (Figure 2.1A). Note the inhibition of the H-reflex when conditioned by the MG stimulus. Conditioning stimuli to the MG nerve resulted in a significant, early inhibition of the soleus H-reflex in 10 of the 15 subjects studied in quiet sitting (Figure 2.2A). One to four conditioning pulses were needed to generate the inhibition in most subjects. The maximum amount of inhibition varied from 5% to 28% of the control reflex. The duration of the inhibition was short-lived, usually seen at a condition-test interval of between 2 to 9 ms, as would be expected of the disynaptic inhibition (Pierrot-Deseilligny et al, 1979).

There was variation between subjects in the strength of the inhibition and the condition-test interval that showed the greatest inhibition of the H-reflex. The difference in timing is not unexpected, since there was some variation in the distance separating the stimulating electrodes for the MG and tibial nerves. Two examples illustrating these differences are shown in Figure 2.3, where the subject shown in B exhibited a very mild degree of inhibition in contrast to the subject in A.

When the results of the 10 subjects were pooled together, the inhibition of the reflex was significant for condition-test intervals of 5 to 9 ms (Figure 2.2A). There was no apparent inhibition or excitation seen at the other condition-test intervals. There was a tendency for the H-reflex to be inhibited at the 1 ms condition-test interval. This inhibition was not significant,

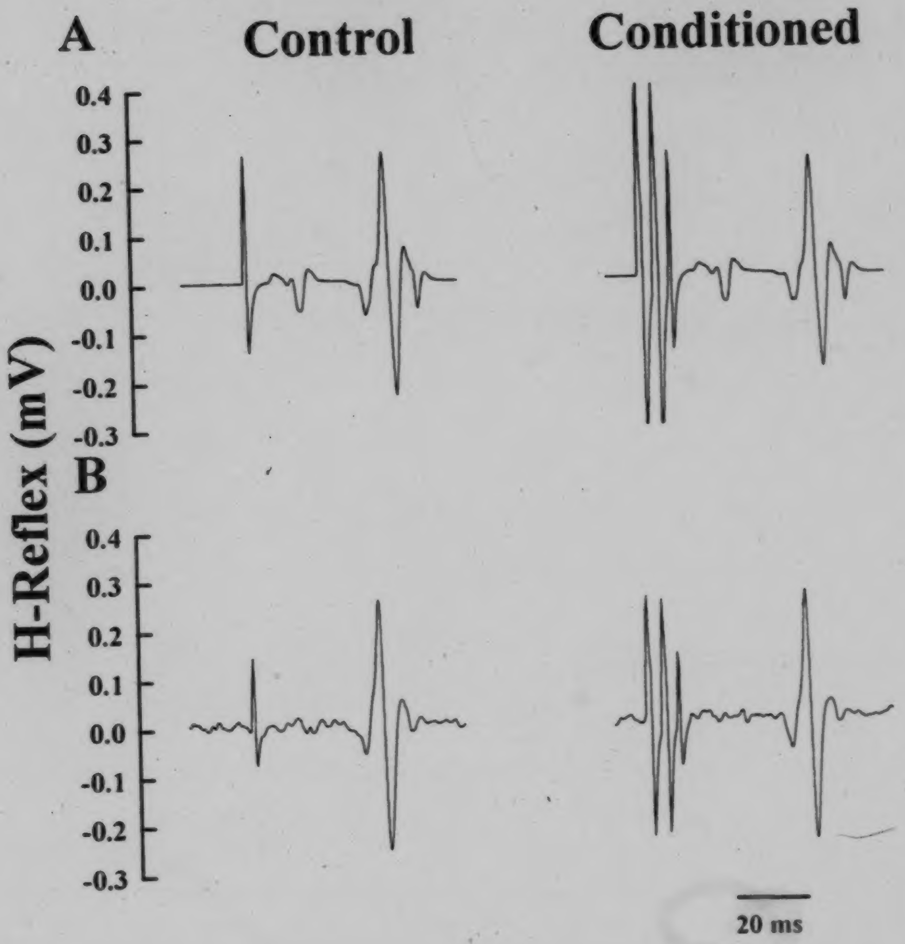

Figure 2.1. The amplitude of the control and conditioned soleus H-reflex is shown for one subject at a condition-test interval of 5 ms, for quiet sitting (**A**) and walking (**B**). Note that the conditioning stimulus to the MG nerve reduces the H-reflex amplitude in quiet sitting (**A**), and the same stimulus has no effect during walking (**B**). In this subject, the conditioning stimulus to the MG nerve consisted of two pulses (note stimulus artifacts). Each of these traces were generated from an average of 20 sweeps in **A** and 40 sweeps in **B**.

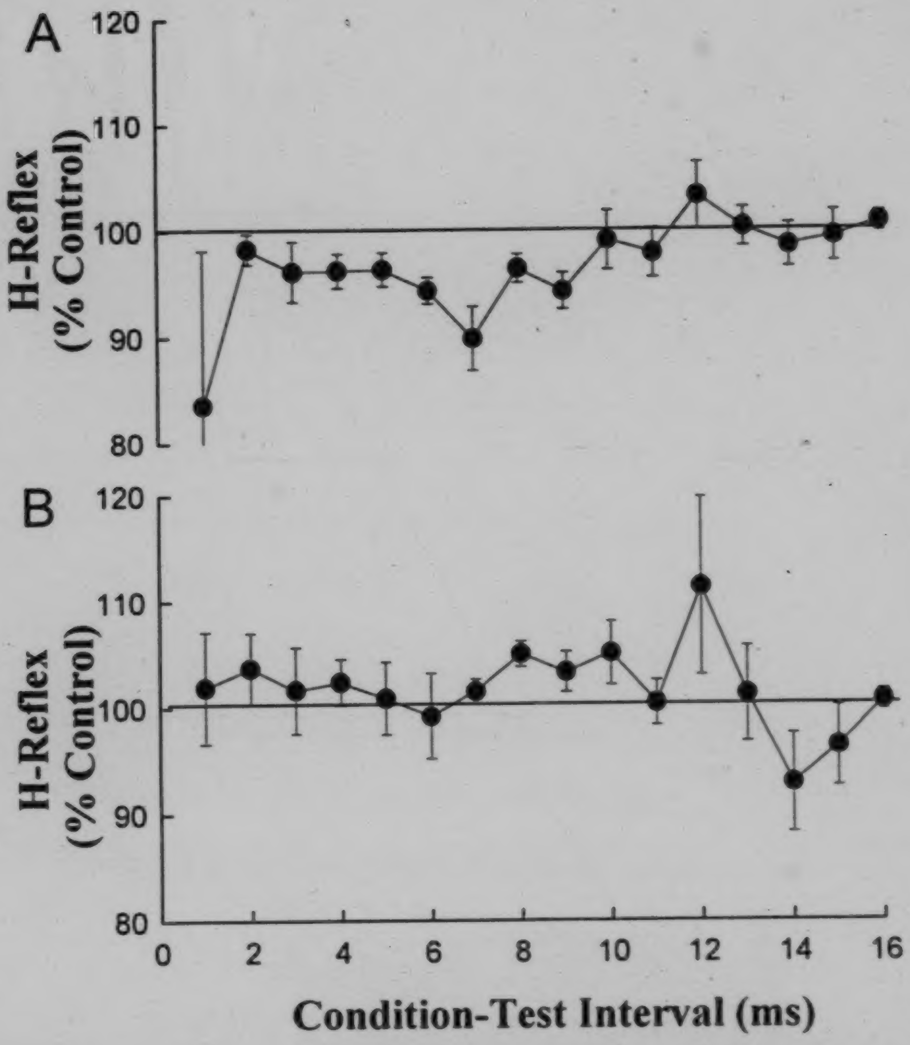

Figure 2.2. The amplitude of the H-reflex when conditioned by prior stimuli to the medial gastrocnemius nerve is shown as a percentage of the control H-reflex, for condition-test intervals of 1 to 16 ms. The data were obtained from 10 subjects, in quiet sitting. The average across subjects is shown with one standard error bar. These 10 subjects showed a significant, early inhibition between 5 and 9 ms (**A**), and 5 subjects showed no significant inhibition or excitation (**B**).

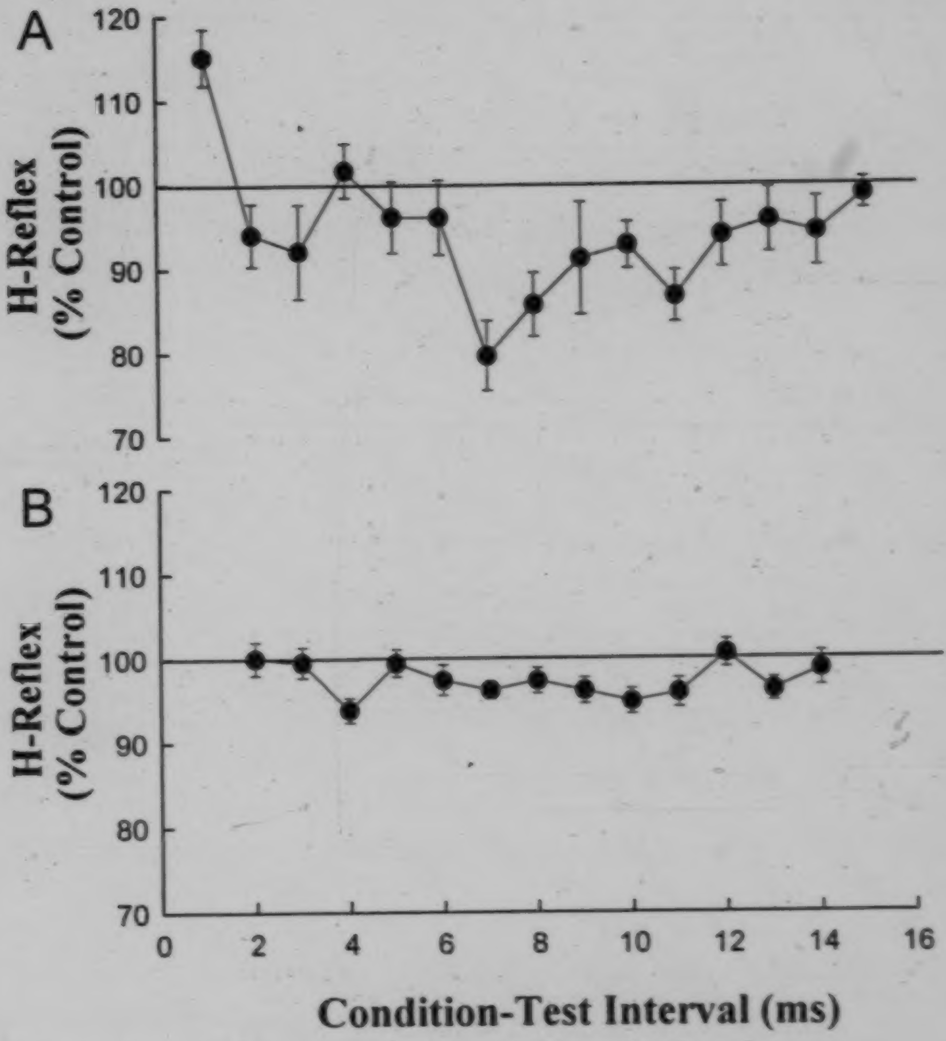

Figure 2.3. The amplitude of the H-reflex when conditioned by prior stimuli to the medial gastrocnemius nerve in quiet sitting is shown for two individuals. The convention of the graph is the same as Figure 2. Each data point represents the average of approximately 30 trials in **A** and approximately 20 trials in **B**. The subject shown in **A** exhibited substantially more inhibition than the subject shown in **B**. The variability of the reflex was also substantially less in **B** than in **A**.

but reminiscent of that reported by Gritti and Schieppati (1989). These very early effects will not be discussed further, as it is beyond the scope of this study. Five subjects showed no significant inhibition under resting conditions; their data are shown in Figure 2.2B.

Isometric contraction of the triceps surae decreased the inhibition

Submaximal isometric contraction of the triceps surae muscle group resulted in a significant reduction of the Ib inhibition at only one of the condition-test intervals (7 ms) in the 9 subjects tested (Figure 2.4B). These 9 subjects are from the original group of 10 that showed a significant inhibition under resting conditions (one subject was not available for testing under the isometric condition).

Standing did not result in further changes to the reflex

In the 5 subjects that were tested on another occasion, the effect of standing was examined by comparing the reflex inhibition under two conditions: sitting and standing, both with a low level (20% maximum) of isometric contraction. The differences were not significant. Thus, the changes in sensory input associated with standing did not affect the reflex.

Reduced inhibition of the H-reflex during walking

The soleus H-reflex was less inhibited by the stimulus to the MG nerve during walking compared to quiet sitting. Example from a single subject is shown in Figure 2.1B. Note that the size of the control H-reflex was the same for quiet sitting and walking, but the effective stimulus strength needed to generate this H-reflex was different (as seen from the size of the M-wave preceding the H-reflex). The difference between quiet sitting and walking was significant ($p<0.05$) at condition-test intervals of 4, 5, 6, and 8 ms in the 10 subjects that showed an inhibition of the reflex under resting conditions (Figure 2.4A). As a group, however, the amplitude of the conditioned H-reflex during walking was not significantly excited. Four out of these 10 subjects showed a significant excitation of the conditioned H-reflex during walking at at least one condition-test interval in the disynaptic range. Their data are shown in Figure 2.5A. Interestingly, these 4 subjects did not show the same excitation during isometric contractions of the triceps surae (Figure 2.5B). This suggests that in these 4 subjects, walking lead to a greater amount of excitation not evident under submaximal isometric contraction. Subjects who did not show an inhibition of the H-reflex with conditioning stimuli at rest did not show any changes in walking (results not shown).

Increasing the number of conditioning pulses did not result in more excitation during walking

The changes observed in the reflex during walking were rather modest, and no changes were seen at longer condition-test intervals. Longer sequences of conditioning pulses were applied in 2 subjects to determine if the effect could be enhanced, particularly at the longer condition-test intervals. The results indicated that the effect could not be enhanced by an increase in the number of conditioning pulses up to 7.

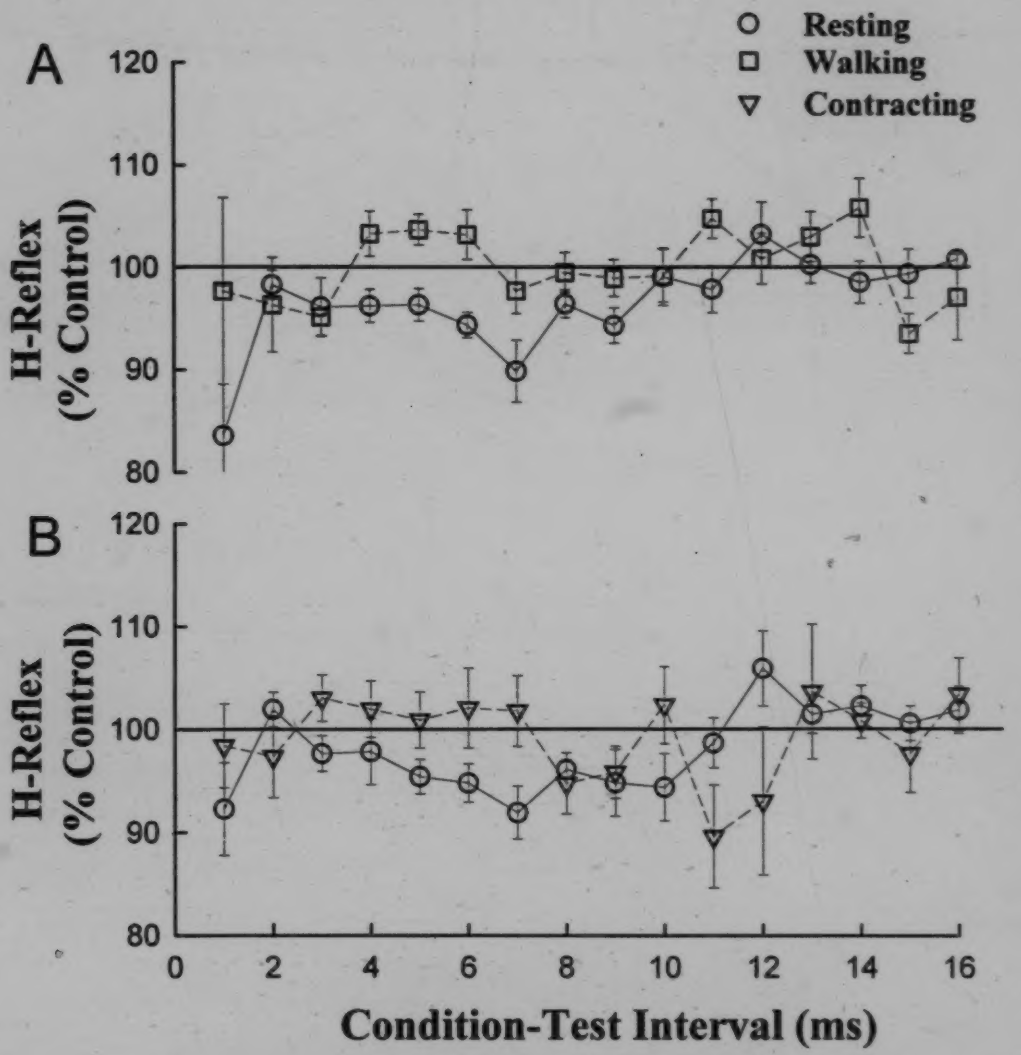

Figure 2.4. A. The amplitude of the H-reflex when conditioned by stimuli to the medial gastrocnemius nerve is shown for quiet sitting (open circles and solid line) and walking (open squares and dashed line). The convention of the graph is the same as Figure 2. The data were obtained from the 10 subjects who showed an early inhibition under resting conditions. Statistically significant differences were observed at condition-test intervals of 4, 5, 6 and 8 ms. The data obtained from 9 of the 10 subjects from **A** are shown in **B** during quiet sitting and submaximal isometric contractions (open triangles and dashed line). The difference was significant at a condition-test interval of 7 ms only.

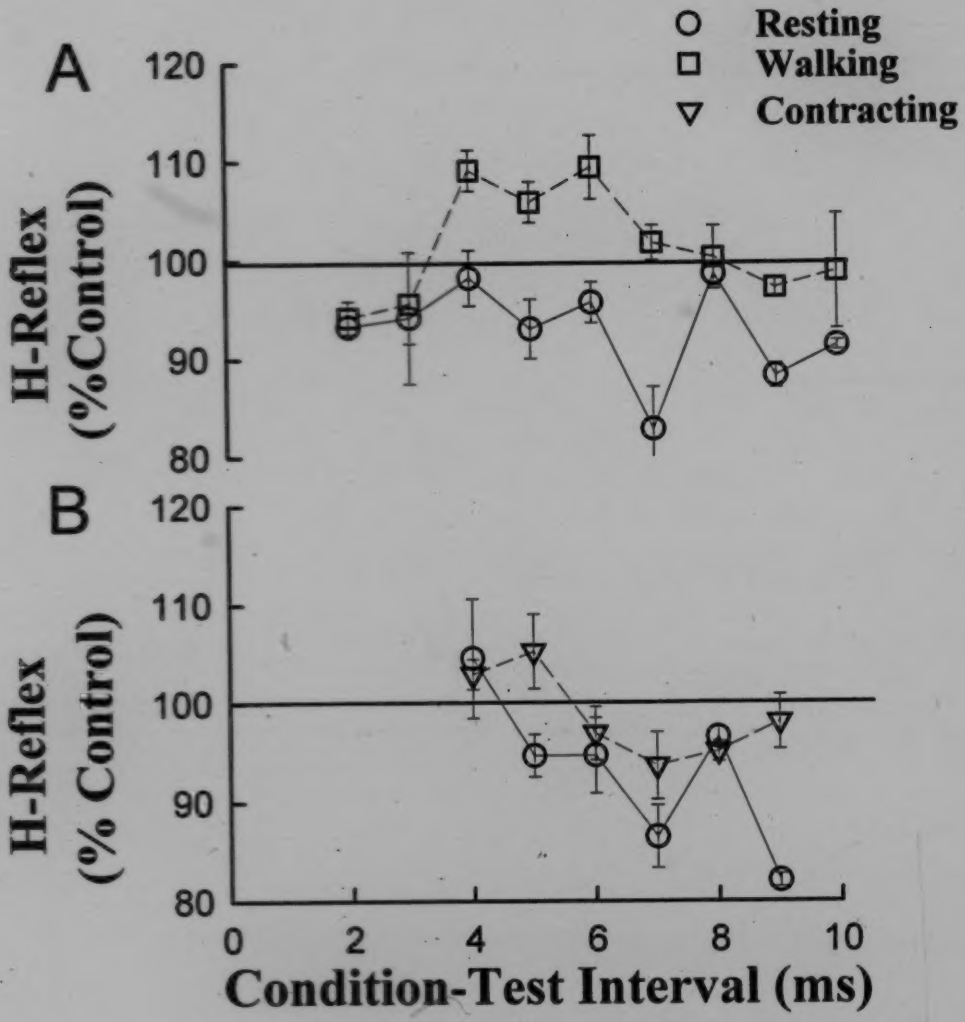

Figure 2.5. Four of the 10 subjects (from Figure 4) showed a significant ($p<0.1$) excitation of the conditioned H-reflex during walking at short condition-test intervals. Data obtained from these 4 individuals are compared for the following conditions: **A** when at rest and during walking, and **B** when at rest and during isometric contractions in sitting. Note that the excitation seen during walking was not as evident during submaximal isometric contractions.

2.4 DISCUSSION

The primary new finding is that the inhibition of the soleus H-reflex, caused by a conditioning stimulus to the MG nerve in sitting, is reduced or reversed to excitation when walking. This was seen at short condition-test intervals, consistent with results on the disynaptic group I reflex from animal work (McCrea et al, 1995).

Group I inhibition in sitting was moderate

The majority of subjects (10 out of 15) showed some early inhibition of the soleus H-reflex in response to conditioning stimuli from the MG nerve in sitting (Figure 2.2A). The inhibition was significant ($p<0.05$) for condition-test intervals of 5 to 9 ms. The results are generally consistent with previous studies in humans, when the differences in methodology are considered. The data presented in two previous publications were derived from single subjects (Figure 1 from Pierrot-Deseilligny et al, 1979, and Figure 1 from Pierrot-Deseilligny et al, 1981). Some subjects from the current study also exhibited a similar or even greater degree of inhibition (e.g., Figure 2.3A). This was, however, not the norm. Most subjects exhibited a very moderate degree of inhibition.

One of the factors which affected the degree of inhibition observed was the sequence of stimulus presentation. When the conditioned reflexes were elicited in succession, the inhibition was greater than when the conditioned reflexes were interspersed with control reflexes. This difference can be fairly marked. Thus, cumulative effects appeared to complicate the interpretation of the results when stimuli were applied in succession. Since slow, time dependent effects were not of interest, we chose to use sequences of trials in which the control and conditioned pulses were applied alternately. Interestingly, the sequence of stimuli presentation used here was most similar to that used by Gritti & Scheippati (1989), whose results are also most similar to ours (contrast with Delwaide, Pepin, and Maertens de Noordhout, 1991; Pierrot-Deseilligny et al., 1979; Pierrot-Deseilligny et al, 1981).

Whatever the reason, a number of subjects (33%) failed to show any inhibition of the H-reflex in sitting. The prevalence of this phenomenon is unclear from the previous studies. The conclusion that Ia afferent projections from the MG muscle to the soleus is weak or absent in primates is based on electrophysiological evidence (Hongo et al, 1984; Pierrot-Deseilligny et al, 1979). It is impossible to rule out the contribution of Ia afferents. Considerable convergence of Ia and Ib effects exists in reduced preparations of the cat during rest (Jankowska, 1992; Jankowska, Johannisson, and Lipski, 1981). Both group Ia and Ib afferents contribute to the short latency effects seen during fictive locomotion (McCrea et al, 1995). Perhaps the individuals who did not exhibit any inhibition had a stronger excitatory contribution from the Ia afferents of the MG muscle to the soleus.

Group I inhibition was reduced in walking

The degree of inhibition caused by the conditioning stimulus to the MG nerve was reduced during walking, at condition-test intervals of 4, 5, 6, and 8 ms. Hence, there appears to be a change in the strength of this short latency, presumably disynaptic, reflex pathway when the subjects were walking. The direction of the change, a reduction in the inhibition and an excitation in some subjects (Figures 2.4A and 2.5A), is consistent with the results from animal work (McCrea et al, 1995).

The strength of the group I input from extensor muscles appeared to depend on the type of preparation in the cat. In spinal fictive locomotor preparations, the group I inhibition seen at rest was reduced or eliminated but no excitation was apparent (McCrea et al, 1995). In contrast, in MLR fictive locomotor preparations, group I input resulted in clear excitation during the extensor phase of the fictive step cycle (McCrea et al., 1995). It was suggested that disynaptic excitation may require supraspinal input. Results from this study indicate that short latency excitation is apparent in some intact humans, but as a group, the effect is not significant.

A number of possibilities could account for the modest effects seen here. First, the current results reflect the strength of group I afferents from a single extensor muscle. The strength of the group I input is muscle dependent (Guertin et al, 1994; Whelan, Hiebert and Pearson, 1995). Perhaps the effect of stimulating the MG nerve is smaller than the effect of stimulating other extensor nerves. Unfortunately, we are limited by the anatomical peculiarities of the human to study this particular nerve-muscle combination (e.g., Bouaziz et al, 1975; Hongo et al, 1984; Mao et al, 1984; Pierrot-Deseilligny et al, 1979).

Second, the current results were obtained from intact human subjects. There may be some fundamental differences in the strength of these effects in reduced cat preparations and in normal behaving animals. The limbs were extensively denervated in most of the studies on cats (Conway et al, 1987; Gossard et al, 1994; Pearson, Raminez, and Jiang, 1992; Pearson and Collins, 1993; Whelan et al, 1995) and in some cases, the animals were immobilized (Gossard et al, 1994; McCrea et al, 1995). Such extensive removal of afferent input could make the rhythm generating network more susceptible to the remaining input. There is likely considerable convergence of information in intact systems. Convergence of afferent input indicating loading may be necessary for the system to respond. Normal loading of a limb would activate not only Ib afferents from many extensor muscles, but also many other afferents such as cutaneous receptors of the foot, and other load sensitive receptors in bone and joints. Indeed, activation of cutaneous receptors from the plantar surface of the foot also enhanced extensor activity in the cat (Guertin et al, 1994). Activating only Ib afferents from one muscle may be inadequate to generate a typical loading response.

Third, the walking was generated by a reduced circuitry in the cat (spinal or brainstem and spinal). The reinforcement of extensor activity by Ib afferents from extensor muscles may be a property of the limited circuitry examined. Perhaps the influence of higher centres in the normal human overshadow these effects. Differences are certainly seen between fictive and walking preparations in the cat. The ability of the stimulus to reset the locomotor rhythm, and to enhance the amplitude of extensor activity is weaker in decerebrate, walking cats (Whelan et al, 1995). In the biped human, careful control of the loading and unloading of the lower limbs is especially important to prevent a fall. Corrective responses that will alter the locomotor rhythm may depend on a more meaningful convergence of sensory input. Artificial loading of a single muscle, as performed here, may not be adequate for the locomotor system to alter its course.

Previous reports in humans (Fournier, Katz and Pierrot-Deseilligny, 1983) have shown modest reduction in the conditioned H-reflex during isometric contractions of moderate intensity, as confirmed here. The reduction in inhibition seen during walking could be partly accounted for by the contraction of the triceps surae muscle group. In some individuals, however, walking resulted in significant excitation of the conditioned H-reflex, over and above that seen during isometric contractions (Figure 2.5).

Results from reduced preparations in the cat indicate a powerful, long latency effect from the Ib afferents on the locomotor rhythm. Gossard and colleagues (1994) estimated the central latency of this effect to be about 3.5 to 4 ms in the cat. No evidence for these longer latency effects were seen here. The long latency effects seen in the cat also required considerable temporal summation, however, so trains of pulses longer than the 7 tried here may be needed. Studies employing a systematic search for the longer latency effects will be needed.

2.5 REFERENCES

Bassler, U., 1976. Reversal of a reflex to a single motorneuron in the stick insect Carausius morosus. *Biol. Cybern. 24*: 47-49.

Bouaziz, Z., Bouaziz, M. and Hugon, M., 1975. Modulation of soleus electromyogram during electrical stimulation of medial gastrocnemius nerve in man. *EEG Clin. Neurophysiol. 15*: 31-42.

Conway, B.A., Hultborn, H. and Kiehn, O., 1987. Proprioceptive input resets central locomotor rhythm in the spinal cat. *Exp. Brain Res. 68*: 643-656.

Crone, C., Hultborn, H., Mazieres, L., Morin, C., Nielsen, J., Pierrot-Deseilligny, E., 1990. Sensitivity of monosynaptic test reflexes to facilitation and inhibition as a function of the test reflex size: a study in man and the cat. *Exp. Brain Res. 81*: 35-45.

Delwaide, P.J. and Oliver, E., 1988. Short-latency autogenic inhibition (IB inhibition) in human spasticity. *J. Neurol. Neurosurg. Psychiatry, 51*: 1546-1550.

Delwaide, P.J., Pepin, J.L. and Maertens de Noordhout, A., 1991. Short-latency autogenic inhibition in patients with Parkinsonian rigidity. *Ann. Neurol. 30*: 83-89.

Duysens, J. and Pearson, K.G., 1980. Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Res. 187*: 321-332.

Eccles, J.C., Eccles, R.M. and Lundberg, A., 1957. Synaptic actions on motorneurones by impulses in Golgi tendon organ afferents. *J. Physiol. 138*: 227-252.

Fournier, E., Katz, R. and Pierrot-Deseilligny, E., 1983. Descending control of reflex pathways in the production of voluntary isolated movements in man. *Brain Res. 288*: 375-377.

Gossard, J-P., Brownstone, R.M., Barajon, I. and Hultborn, H., 1994. Transmission in a locomotor-related group Ib pathway from hindlimb extensor muscles in the cat. *Exp. Brain Res. 98*: 213-228.

Gritti, I. and Schieppati, M., 1989. Short-latency inhibition of soleus motorneurones by impulses in Ia afferents from the gastrocnemius muscle in humans. *J. Physiol. (Lond.) 416*: 469-484.

Guertin, P., Angel, M.J., Jimenez, I. and McCrea, D.A., 1994. Both disynaptic and longer latency interneuronal pathways mediate extension enhancement evoked by group I muscle afferents during fictive locomotion. *Soc. Neurosci. Abstr. Vol. 20 Part 2*: p.1582.

Hongo, T., Lundberg, A., Phillips, C.G. and Thompson, R.F., 1984. The pattern of monosynaptic Ia-connections to hindlimb motor nuclei in the baboon: a comparison with the cat. *Proc. R. Soc. Lond. B 221*: 261-289.

Hugon, M., 1973. Methodology of the Hoffman reflex in man. In: J.E. Desmedt (Ed.), *New Developments in Electromyography and Clinical Neurophysiology. Vol. 3*, Karger:Basel, pp. 277-293.

Jankowska, E., 1992. Interneuronal relay in spinal pathways from proprioceptors. *Prog. Neurobiol. 38*: 335-378.

Jankowska, E., Johannisson, T. and Lipski, J., 1981. Common interneurones in reflex pathways from group Ia and Ib afferents of ankle extensors in the cat. *J. Physiol. 310*: 381-402.

Keppel, G., 1982. *Design and Analysis: A Researcher's Handbook. Second edition*, Prentice-Hall: New Jersey.

Laporte, Y. and Lloyd, D.P.C., 1952. Nature and significance of the reflex connections established by large afferent fibres of muscular origin. *Am. J. Physiol. 169*: 609-621.

Mao, C.C., Ashby, P., Wang, M. and McCrea, D., 1984. Synaptic connections from large muscle afferents to the motorneurons of various leg muscles in man. *Exp. Brain Res. 56*: 341-350.

McCrea, D.A., Shefchyk, S.J., Stephens, M.J. and Pearson, K.G., 1995. Disynaptic group I excitation of synergist ankle extensor motorneurons during fictive locomotion. *J. Physiol. 487*: 527-539.

Meinck, H.M., 1980. Facilitation and inhibition of the human H-reflex as a function of the amplitude of the control reflex. *EEG Clin. Neurophysiol. 48*:203-211.

Pearson, K.G., Ramirez, J.M. and Jiang, W., 1992. Entrainment of the locomotor rhythm by group Ib afferents from ankle extensor muscles in spinal cats. *Exp. Brain Res. 90*: 557-566.

Pearson, K.G. and Collins, D.F., 1993. Reversal of the influence of group Ib afferents from plantaris on activity in medial gastrocnemius muscle during locomotor activity. *J. Neurophysiol. 70*: 1009-1017.

Pierrot-Deseilligny, E., Katz, R. and Morin, C., 1979. Evidence for Ib inhibition in human subjects. *Brain Res. 166*: 176-179.

Pierrot-Deseilligny, E., Morin, C., Bergego, C. and Tankov, N., 1981. Pattern of group I fibre projections from ankle flexor and extensor muscles in man. *Exp. Brain Res. 42*: 337-350.

Skorupski, P. and Sillar, K.T., 1986. Phase-dependent reversal of reflexes medicated by the thoracocoxal muscle receptor organ in the crayfish, Pacifastacus leniusculus. *J. Neurophysiol, 55*: 689-695.

Stein, R.B. and Capaday, C., 1987. The modulation of human reflexes during functional motor tasks. *Trends Neurosci. 11*: 328-332.

Stephens, M.J. and Yang, J.F., 1994. Autogenic (Ib) inhibition in sitting and walking in humans. *Soc. Neurosci. Abstr, Vol 20, part 2*: p.1583.

Taborikova, H. and Sax, D.S., 1969. Conditioning of H-reflexes by a preceding subthreshold H-reflex stimulus. *Brain 92*: 203-212.

Whelan, P.J., Hiebert, G.W. and Pearson, K.G., 1995. Stimulation of the group I extensor afferents prolongs the stance phase in walking cats. *Exp. Brain Res. 103*: 20-30.

3.0 LOADING DURING THE STANCE PHASE OF WALKING IN HEALTHY, ADULT HUMANS*

3.1 INTRODUCTION

Recent work in decerebrate and spinal cats has confirmed that group I sensory input from extensor muscles helps control the duration of the stance phase in walking. For example, enhanced group I input from extensor muscles increases the amplitude and duration of the extensor electromyographic (EMG) burst associated with the stance phase, and delays the onset of the subsequent swing phase. This is true of group I input from electrical stimulation of the muscle nerve (Conway et al. 1987; Pearson & Collins 1993; Guertin et al. 1995), direct stretch to the muscle (Duysens & Pearson 1980; Guertin et al. 1995), or vibration of the muscle tendon (Guertin et al. 1995). These same afferents can entrain the locomotor rhythm (Conway et al. 1987; Pearson et al. 1992), providing further evidence for their access to the rhythm generator itself. The presumed functional significance of these results is that afferent activity from extensor muscles in the supporting limb: a) increases support in response to increased load, and b) prolongs the stance phase until unloading of the limb has occurred.

Do group I afferents from extensor muscles have a similar function in the intact human? Intuitively, signals that indicate the readiness of a limb to progress to the swing phase from the stance phase should be especially important for a biped, whose postural stability is easily disrupted. In an earlier report, the behaviour of a putative group Ib reflex in extensor muscles at the ankle was studied during sitting and walking. During walking, the inhibition produced by afferents from the medial gastrocnemius nerve in the soleus muscle was decreased (Stephens and Yang, 1996a), but the change from sitting to walking was small. Moreover, no excitation was found at longer latencies, in direct contrast to results in the cat (Pearson & Collins 1993; Gossard et al. 1994; Guertin et al. 1995). One possible explanation for this small effect is that we were using an artificial, electrical stimulus to one muscle nerve. Johansson and Westling (1987) have shown that reflex response to artificial stimuli in the intact human can be reduced if the subject is aware of its presence and benign nature. Moreover, afferent input from some muscles may be weaker than others (Whelan et al., 1995; Fouad & Pearson 1997). Perhaps the afferents from the medial gastrocnemius muscle do not have a strong influence on the soleus motorneurons.

---

* The study included in this chapter is published in: Stephens, M.J. and Yang, J.F., (1999). Loading during the stance phase of walking in humans increases the extensor EMG amplitude with little change in timing of the step cycle. Exp. Brain Res. 124(3): 363-370. Contribution to paper: Involved with the development of the protocol, recruitment of subjects, pilot testing, data collection, data and statistical analyses, development of the figures and initial draft of the paper.

The amplitude and duration of the extensor EMG burst increase with increasing load during walking in the adult human, for loads less than body weight (Finch et al. 1991; Harkema et al. 1997). Unloading in these studies was achieved by raising the subject with a harness (Finch et al. 1991). This form of unloading decreases the maximum contact distance over which the foot can make contact with the treadmill. Thus, the changes in timing may have resulted largely from this mechanical effect. Others have added loads to the body. These loads were added to the hands, front or back of the trunk (Eke-Okoro & Larsson 1984; Ghori & Luckwill 1985; Simonsen et al. 1995). The muscle responses to such loads are confounded by postural adjustments that are necessary to stay balanced.

In our recent study of supported walking in the human infant, we added load directly by changing the amount of weight supported by the infant (Yang et al. 1998). Adding a load of approximately 22% of the infant's body weight increased both the duration of the stance phase (30%) and step cycle (28%). The amplitude of the EMG from extensor muscles (quadriceps and gastroc-soleus) did not change. These results confirmed the importance of load in controlling the stepping rhythm, at least for the immature human.

The current study was designed to avoid problems of artificial stimuli and differential potency of afferents from different muscles. We added or removed loads directly to the walking subjects, similar to the study on infants. Load was applied near the centre of mass to avoid the problem of postural adjustments. We tested whether loading during the stance phase prolongs the stance phase and delays the onset of swing. We used both sudden, unexpected changes in load, and sustained changes in load over the entire trial. Adding loads in this way, of course, activates many types of afferents originating from muscle, skin, joint and bone. We do not attempt to separate the contribution of these different afferent types in this report. These results have been presented in preliminary form (Stephens and Yang, 1996b).

3.2 MATERIALS AND METHODS

Subjects:

Twenty subjects (23 to 41 years of age) were studied under different conditions of loading and unloading. Approval was obtained from the human ethics committee at the University of Alberta. Informed written consent was obtained from all subjects. Thirteen subjects were studied with either a transient addition or removal of load (equivalent to 30% of body weight), or with a sustained addition of the same weight. Eleven subjects were studied with a sustained removal of 30% body weight using a body harness. Four subjects were studied under both conditions.

Recording Procedures:

Electromyographic data were collected either bilaterally from the soleus (SOL) and tibialis anterior (TA) muscles or unilaterally from the SOL, TA, vastus lateralis (VL) and biceps femoris (BF). Beckman Ag/AgCl surface electrodes, 1 cm in diameter, were placed 1 cm apart rim-to-rim over the muscles. The signals were amplified and band-pass filtered (10 Hz-30 kHz). Footswitches were mounted under the ball and heel of both feet to monitor foot contact. In 2 subjects, force sensitive resistors (FSRs) (Interlink Electronics, Camarillo, CA), 2.5 cm in diameter, were placed under the heel, and under the heads of the first and fifth metatarsals of the left foot, while footswitches were placed beneath the right foot. The FSRs were sandwiched between two metal plates, to improve their accuracy (Zehr et al. 1995). Electrogoniometers (Penny and Giles Inc., Santa Monica, CA) were placed at the ankle and knee joints.

Electrogoniometer signals were amplified and band-pass filtered (0-300 Hz). Data were recorded on magnetic tape (VHS) using the Vetter Digital PCM Recording Adaptor (Model 4000A).

Experimental Procedures:

Loads were applied through a belt (used for mountain climbing, commonly referred to as a climbing harness) worn on the pelvis, with leg straps (Figure 3.1A). An oval metal frame that encircled the subject was attached to the belt with straps. Diving weights were secured to this frame. The combined weight of frame and weights was 30% of the subject's body weight. Thirty percent is a substantial but safe load. The frame was suspended from a cross-bar connected to a pulley system, above the subject's head. The frame could be raised or lowered manually, allowing the subject to support either no extra weight or the full weight of the frame. A load cell, in series with the pulley system, monitored the load. The subject walked on a treadmill at a comfortable walking speed (0.9-1.0 m/s), with: 1) no added weight, 2) added weight for 70 strides, and 3) added weight applied suddenly during the stance phase. In the third condition, the weight remained on the subject for 3 to 10 steps. The load was applied and removed repeatedly at random times throughout a trial. To reduce potential auditory cues associated with loading or unloading, the subjects listened to music through a set of headphones.

To remove 30% body weight, subjects wore a body harness (Production en readaptation et activite physique, Montreal, Quebec) that was suspended on a tripod (Figure 3.1B). A motorized winch controlled the amount of weight supported by the harness. The amount of weight supported by the system was recorded by a load cell. Subjects walked with: 1) harness on but no body weight removed, and 2) 30% body weight removed through the harness/winch system. In the trial with unweighting, the winch was adjusted so that the force equalled 30% of the subject's body weight in standing. The changes in height of the hip were estimated from video in three subjects, using a marker on the greater trochanter.

In addition, the maximum reach of the lower limbs under the 2 conditions was estimated. Subjects stood with weight on one foot, and reached maximally forward and backward in turn. To standardize the measurement, both feet were required to make full contact with the ground.

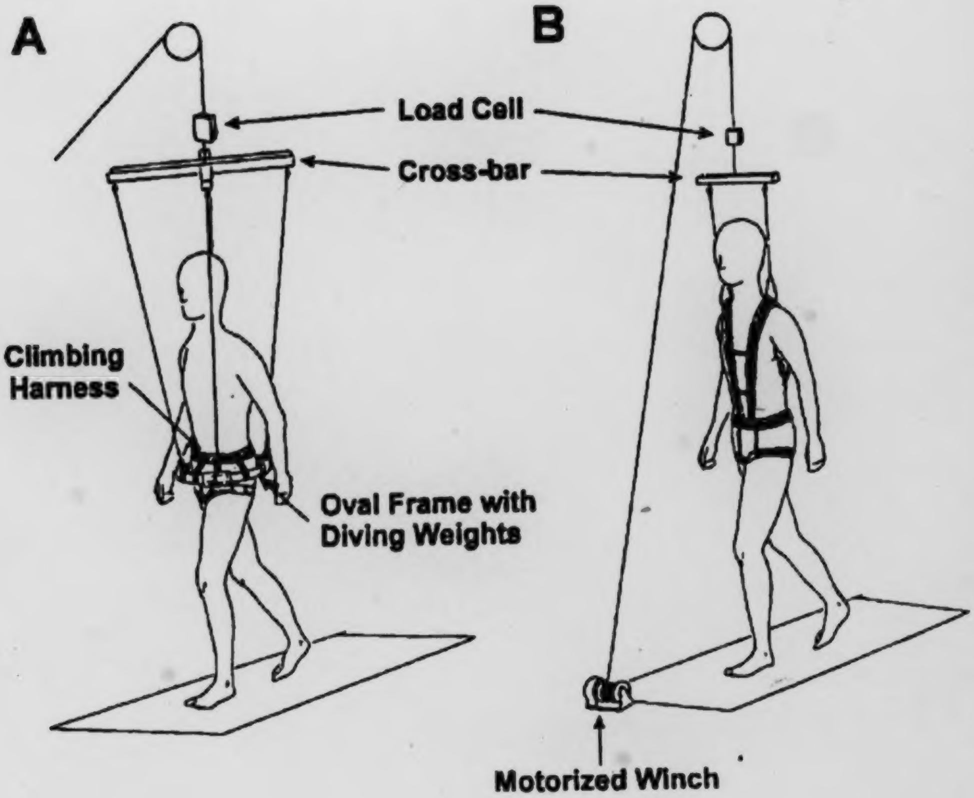
A
B
Load Cell
Cross-bar
Climbing Harness
Oval Frame with Diving Weights
Motorized Winch

Figure 3.1. Schematic diagram of how load was added and removed during walking. A. Illustration of how loads were added. The subject wore a climbing harness, which was attached to the oval frame containing the weights. The oval fraine could be raised (supported by the cross-bar) to give no additional load, or lowered (supported by the subject through the climbing belt) to give loading. B. Illustration of subject in a body harness for experiments in which 30% of body weight was removed. The motorized winch was used to control the amount of unloading. In both A and B, a load ceR monitored the loading condition.

Data Analysis:

The EMG was full-wave rectified and low-pass filtered at 30 Hz, then A/D converted with the footswitch/FSR, force transducer and electrogoniometer data at 350 Hz (Axotape, Axon Instr. Inc., Foster City, CA).

i) Sustained loading or unloading: The walking pattern (i.e., EMG, footswitch or FSR) for sustained loading was obtained by averaging across all the steps (n>70 for each condition). This average was compared with the average of trials in which no extra load was carried. Foot contact provided the trigger for averaging, and averages were obtained for the full step cycle. The magnitude of extensor EMGs during the stance phase was quantified by the average amplitude of the signal during the stance phase (i.e., area under the rectified EMG profile divided by the duration of the stance phase). The muscle was defined as being active when the EMG magnitude exceeded 2 standard deviations of the noise level (this noise level was calculated from periods of inactivity). The burst duration of the SOL during the stance phase was estimated based on the definition of activity above. The SOL was active at the beginning of the stance phase in all subjects, so the duration represented the time from heel-contact to the time the SOL EMG burst terminated.

ii) Transient loading or unloading: The response to transient loading was averaged based on the time at which the load was applied. Each trial was assigned to one of 3 groups, depending on whether it occurred in the first, second or last third of the stance phase. Each group was averaged separately. A minimum of 20 trials were averaged for each group. The amplitude and the duration of the burst were calculated separately. For the calculation of the burst amplitude, the disturbed steps were aligned using the onset of the disturbance. This guarded against the inclusion of responses with different latencies. The trigger for averaging was obtained from the force transducer. The trigger level was set arbitrarily to half the total load (see arrow in bottom trace of Figure 3). The average EMG of normal walking was subtracted from the average EMG during loading (or unloading), to obtain the EMG response to sudden changes in load. The amplitude of the response was defined as the average EMG amplitude during the first 200 ms. The 200 ms time window was chosen because of the relatively slow time course of such disturbances and the additional time needed for the load to be experienced by the muscles of the lower limb.

The duration of the extensor EMG burst was estimated by aligning the disturbed steps using the time of heel-contact. This preserved the timing of the signal. If the disturbances were aligned to the time of onset of the disturbance (as in the calculation of the burst amplitude), there would be a distortion of the timing, because the disturbances could occur at any time within the 1/3 duration of the stance phase (typically over 200 ms in duration).

iii) Calibration of FSRs: The FSRs were calibrated with weights up to 1334 N in increments of 108 N. The calibration values were best fit with a hyperbolic function, reflecting the highly non-linear characteristics of the transducer. The signals from walking were scaled accordingly (see Zehr et al. 1995).

Statistical Analysis:

Data for normal walking and data for sustained changes in load were compared using paired Student's t-tests. Data for transiently applied disturbances during the early, middle or late parts of the stance phase were compared using a repeated-measures ANOVA. The variables considered included the duration of the stance phase and step cycle, the duration and the amplitude of the extensor EMG burst during the stance phase. Bonferroni t-tests were used for post-hoc analysis. The significance level was set at 0.05 for all tests.

3.3 RESULTS

Increase in Load

Walking with sustained increases in load produced significant increases in the magnitude of the extensor EMG during the stance phase. Figure 3.2A shows the extensor EMG from one subject during walking, averaged over many steps. The pooled data from 13 subjects (Figure 3.2B) shows a significant change in the average amplitude of the extensor EMG (14% and 78% for the SOL and VL, respectively). There was also a significant but smaller change in the EMG duration (7% for the SOL). The burst duration of VL was not compared, because some subjects showed no VL activity during normal walking. The stance phase duration was significantly prolonged, but only by a small amount (5%) (Figure 3.2C). The step cycle duration was unchanged (Figure 3.2C), however, since the swing phase duration was significantly shortened. There were no consistent changes in EMG amplitude of the flexors (not shown).

Similar changes were seen with transient loading. Results from a single subject are shown in Figure 3.3, where load was applied transiently during early stance (see decrease in force in bottom trace). The amplitude of both the heel and toe FSRs increased when the load was applied. The extensor EMGs (SOL and VL) increased substantially in amplitude, whereas the burst durations hardly changed (see also Figure 3.4A). The duration of the step cycle was largely unchanged. Pooled across subjects, the amplitude of the extensor EMGs increased when load was applied (Figure 3.4B). Significant increases in amplitude were seen in the SOL EMG, whenever load was applied during the stance phase (40%, 21%, and 59% for early, middle and late, respectively). Amplitude increases were only seen in the quadriceps muscle if loads

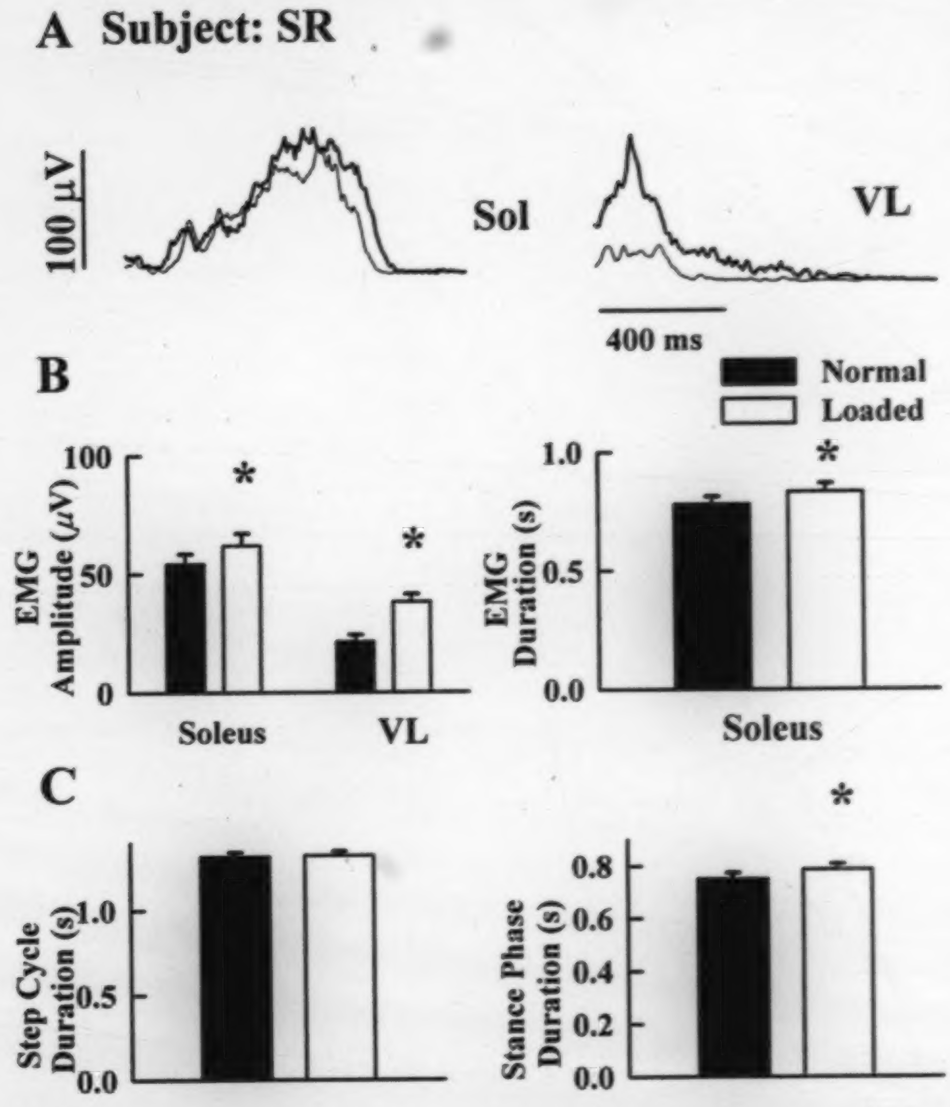

Figure 3.2. Response to loading sustained over the whole trial. **A.** Average extensor EMG (n>70 steps) from one subject walking with no extra load (thin lines) and with additional load equivalent to 30% body weight (thick lines). **B.** Pooled across 13 subjects, the EMG amplitude is significantly increased in both extensors. The duration of the SOL burst is also increased, but less so. **C.** The stance phase duration is significantly increased, whereas the step cycle duration is unchanged.

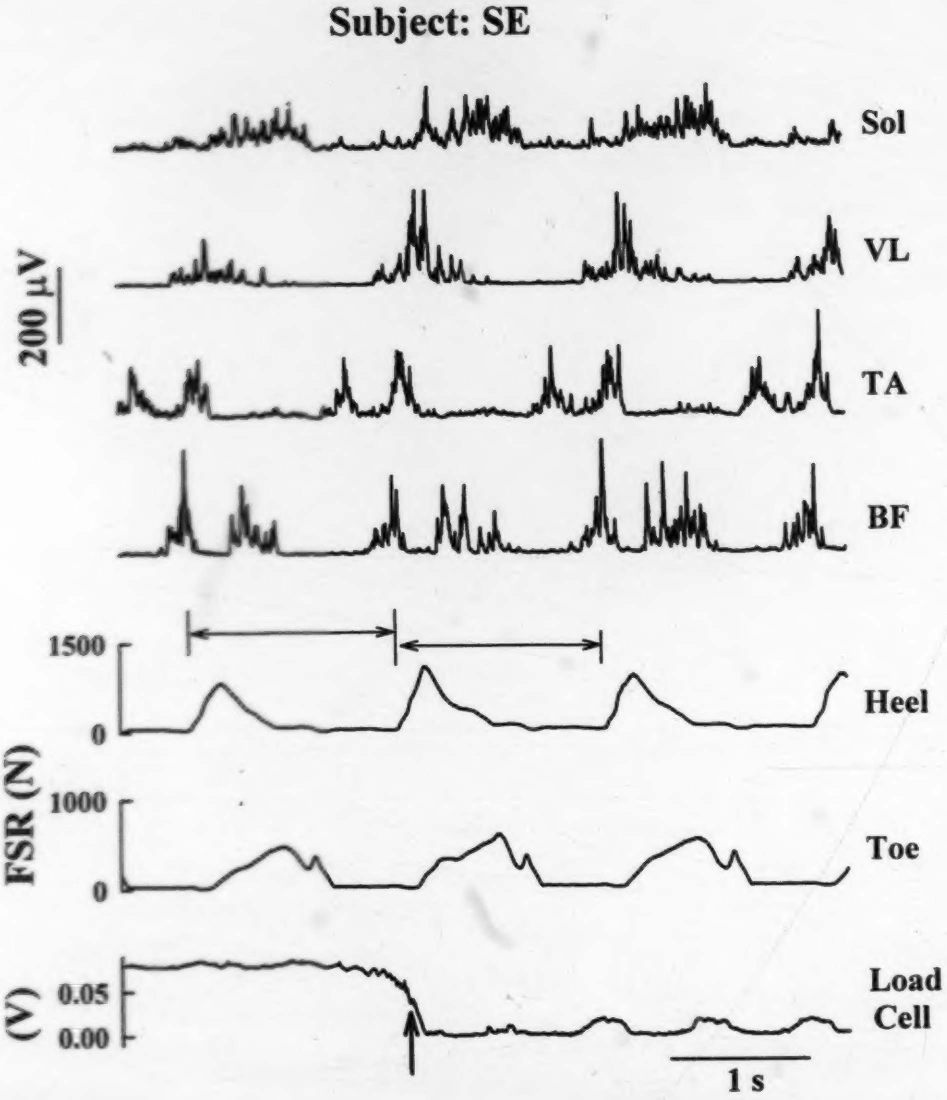

Figure 3.3. Example of EMG and FSR recordings from a single subject during steps preceding, during and following the sudden application of load. The load cell indicates the onset of load application, which was arbitrarily defined as when 50% of the load was applied (arrow). In this case, the load was applied early in the stance phase. The addition of load resulted in an increase in the extensor EMG amplitudes (SOL and VL), with little change in the duration of the step cycle (horizontal bars above the heel FSR signal). There was also no change in the time of onset of TA activity after the disturbance.

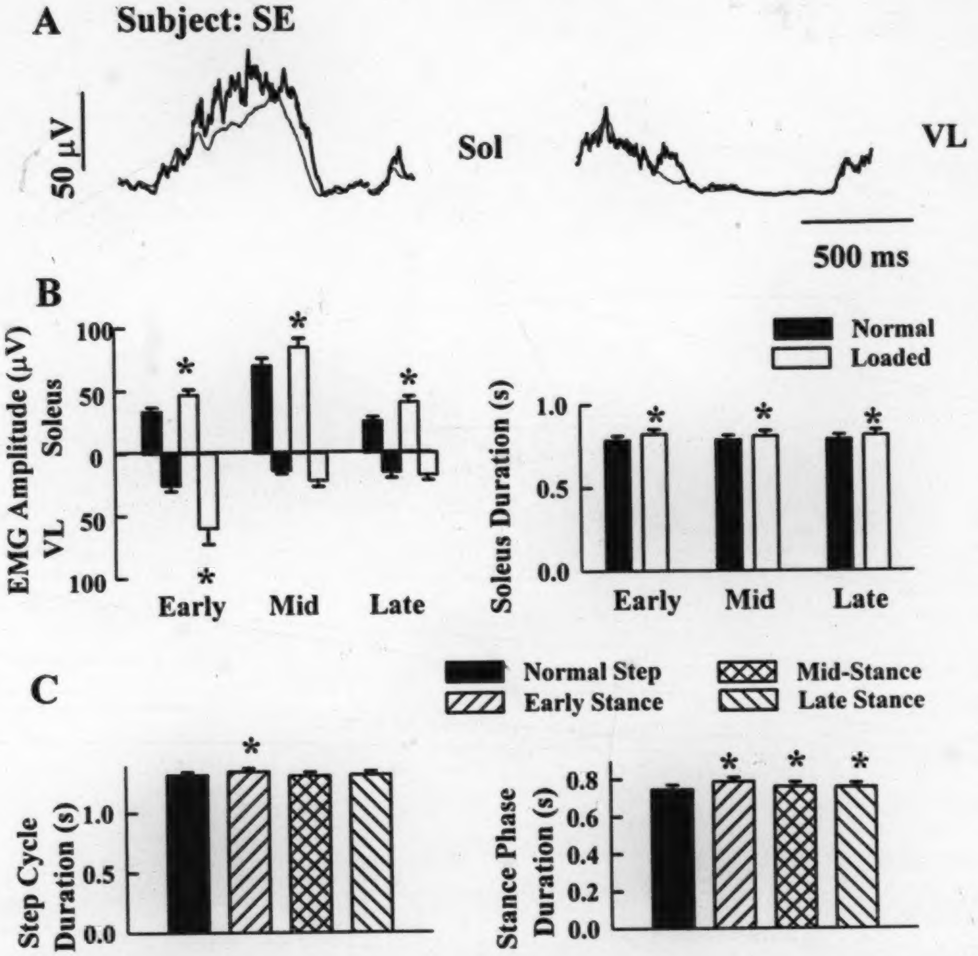

Figure 3.4. Response to a sudden increase in load during the stance phase. **A**: The average EMG pattern from two extensor muscles during normal walking (thin lines, n=523) and when loads were added suddenly during the middle of the stance phase (thick lines, n=22), in one subject. **B.** Pooled across 13 subjects, the SOL EMG amplitude (upward bars on the left) increased significantly (*) with loading, regardless of when the load was applied during stance. The VL EMG (downward bars on the left) increased significantly only when loads were applied early in stance. The duration of the SOL EMG burst (bar graph on the right) increased slightly, but significantly. **C.** The stance phase duration was similarly prolonged, but the changes were small. The duration of the step cycle was significantly prolonged only when disturbances were applied early in the stance phase. The "*" in part C indicates a significant difference from the normal step.

were applied early in the stance phase (average increase was 134%) (Figure 3.4B). Thus, in general, the amplitude of the EMG from extensor muscles increased substantially with load. This effect was strongest when the muscle was most active (i.e., VL in early stance only, while SOL throughout the stance phase). Some differences were found between individuals, however. Four showed little response (< 5 μV) in the SOL muscle, while 2 showed little response in the quadriceps. Most subjects responded with both muscles. The burst duration of the SOL muscle increased slightly (5%, 3% and 3% for early, middle and late, respectively). The stance phase was slightly lengthened (6%, 2% and 2% for early, middle and late, respectively). Cycle duration only changed if the load was applied early in the stance phase (2%, -0.5%, 0% for early, middle and late, respectively).

The response to the first occurrence of the load was compared with the average response to transient loads. No differences were observed in the average amplitude of the extensor EMGs between the first and subsequent applications of load. The stance phase duration was significantly longer for the first loaded step (769 ± 45 ms) compared to the others (746 ± 43 ms), but the difference was small (23 ms). There were no significant differences in the duration of the step cycle.

Onset of the EMG response in the SOL and VL was compared with the onset of changes in ankle and knee angle, respectively. In the majority of cases, the EMG changes preceded changes in joint angle. Thus, it is unlikely that the responses were stretch induced.

Removal of load

When the added load was transiently removed, opposite effects were seen (Figure 3.5). The SOL EMG amplitudes decreased (14%, 6% and 5% for early, middle and late disturbances, respectively). Vastus lateralis EMG amplitudes decreased during early stance only (14%). The soleus burst duration changed significantly only when the load was removed early in the stance phase. The stance phase duration shortened slightly (3%, 2% and 2% for early, middle and late, respectively) (Figure 3.5C). Again, the duration of the step cycle was hardly affected (1% or less) (Figure 3.4C).

Sustained unloading

Sustained removal of 30% body weight by supporting part of body weight with a body harness caused greater changes in step cycle duration. The stance phase shortened by 14%, and the swing phase lengthened, so the total cycle duration was only shortened by 3% (Figure 3.6C). Interestingly, the SOL EMG amplitudes did not change significantly, while the burst duration decreased. Quadriceps EMG was not collected in these subjects.

Supporting body weight with a harness requires lifting the individual. Lifting decreases the distance over which the foot can make contact with the ground (i.e. in the extreme case, no contact can be made). We estimated the change in vertical position of the hip with 30% body-weight support during walking in 3 subjects. The measures were taken at the highest position achieved by the hip joint during walking (the mid-stance phase). The average change in the vertical position of the hip was 2 cm. The maximum reach, defined as the distance between the farthest forward and backward position a foot could be placed, decreased by 38% on average.

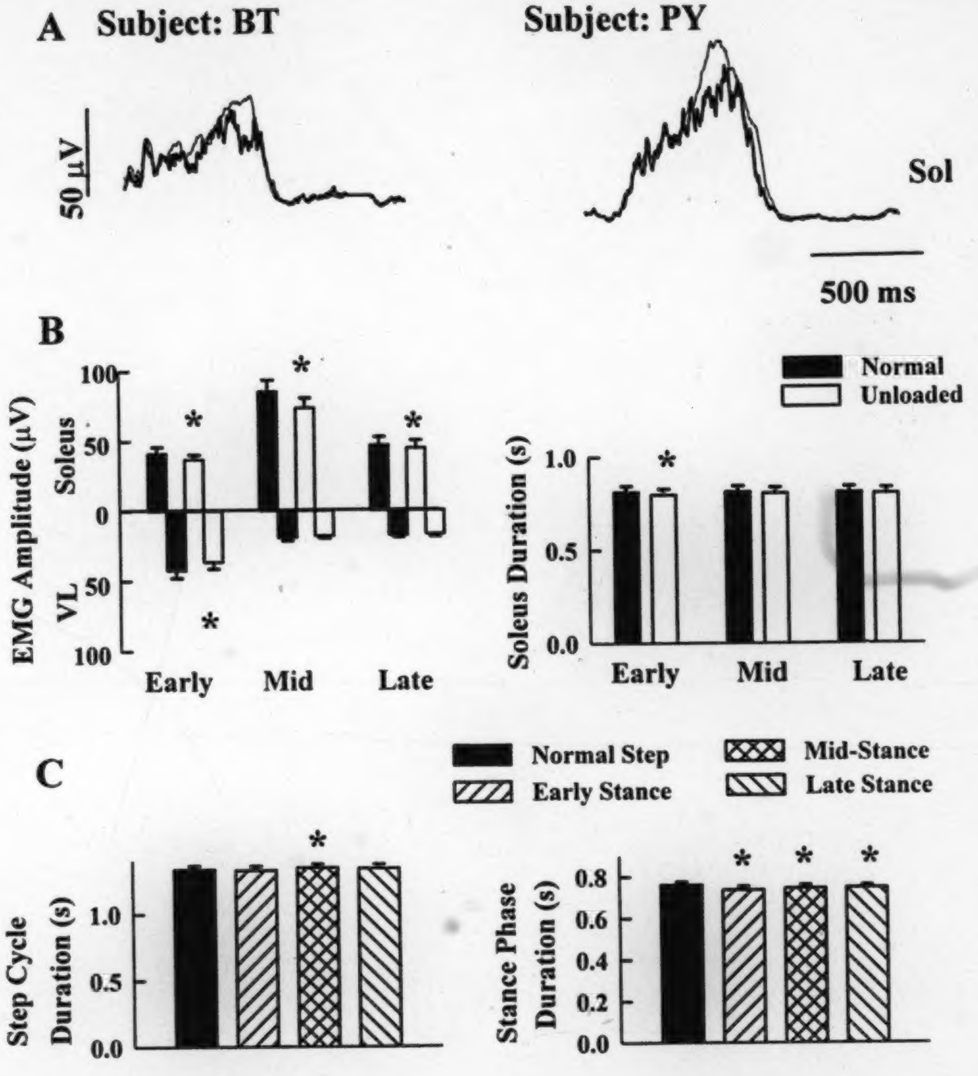

Figure 3.5. Response to the removal of the added weight. **A.** Average SOL EMG during steps with the added weight (thin lines, n>300) and the step when the added weight was removed (thick lines, n>10). **B.** Pooled across subjects, the magnitude of the SOL EMG decreased whenever the load was removed, whereas the VL EMG decreased significantly only when the load was removed early in the stance phase. The burst duration of the SOL was significantly decreased only when loads were removed early in the stance phase. **C.** The duration of the stance phase was significantly decreased. The step cycle duration was relatively unchanged except when the load was removed in the middle of the stance phase.

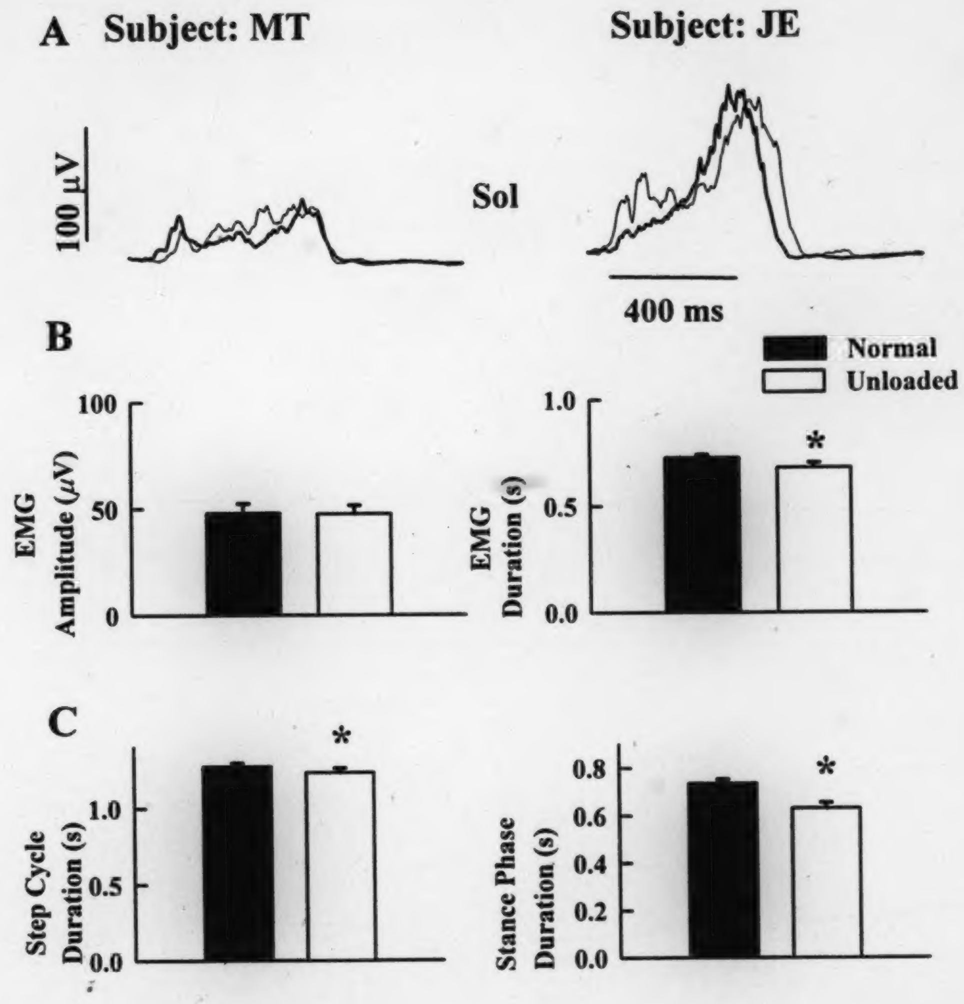

Figure 3.6. Unloading with a body harness. **A.** With 30% of the body weight supported by a harness, the SOL EMG changes were inconsistent between subjects. Thin lines show the average EMG while walking with normal load, and thick lines show it for unloaded walking (n>70). Subject MT showed a decrease in the EMG amplitude with no change in duration, while subject JE showed a small change in magnitude and a decrease in the burst duration. **B.** Pooled across 11 subjects, there was no significant change in the SOL EMG amplitude, but a significant decrease in its burst duration. **C.** The stance phase and step cycle durations were significantly shortened.

3.4 DISCUSSION

This study shows that adding or removing weight from a walking subject during the stance phase changes the amplitude of the EMG from the extensor muscles (especially the quadriceps muscle). The duration of the extensor EMG burst, the stance phase and the step cycle were only slightly changed if at all. The independence of the duration and amplitude of extensor EMG activity in response to load suggests that the subject can control the two independently.

Technical considerations

Walking on a treadmill forces the subject to keep a constant walking velocity. Were the reciprocal changes in the stance and swing phase durations a result of treadmill walking? This is unlikely, since subjects can step at different cadences at the same treadmill speed. At the speeds used here, a six-fold range is possible in both the stance phase and the cycle duration (Nilsson & Thorstensson 1987). Thus, subjects could have modified the duration of the step cycle, but chose not to do so. Whether overground walking would produce the same results remains unknown.

Removing body weight had the greatest effect on the duration of the stance phase and step cycle (Figure 3.6). Unloading using a body harness requires raising the body. Our estimate of 2 cm rise in the position of the hip is similar to that reported by others (1.5 cm in Finch et al. 1991). This rise decreased the maximum reach of the lower leg by an average of 38%. This effect presumably caused the shortening of the step length reported by Finch et al. (1991). This effect may also explain the greater change in stance phase and step cycle duration. Thus, the change in stance phase and step cycle duration with unloading is not a purely neural phenomenon.

Does the predictability of changes in load make a difference?

We studied both sustained and sudden changes in load, because the response to a known and continuous load might be different from the response to an unpredictable one. Moreover, the very first trial in which load was applied should constitute a truly novel task, and might be expected to elicit a different response from subsequent trials. The differences, however, were very small. There were no significant differences between the first and subsequent trials in the magnitude of the EMG response. Subjects modified the amplitude of the EMG burst with both continuous and sudden applications of load. The duration of the stance phase was significantly longer in the first trial compared to subsequent trials, but the difference was very small (23 ms).

Changes in amplitude and timing

Changes in load produced larger changes in the amplitude of the VL EMG than the SOL. This was true for both sustained and sudden changes in load. This difference between the muscles may be related to the role of these muscles in walking. The SOL in cats and humans is very active in standing and slow walking whereas the VL is not (Smith et al. 1977, Walmsley et al. 1978, Yang & Winter 1985, Duysens et al. 1991). This activity pattern matches the fibre type composition, as SOL is composed largely of slow twitch fibres whereas the VL is composed largely of fast twitch fibres (Johnson et al. 1973, Edgerton et al. 1975). With increasing task demand, such as with increasing walking speeds, walking on inclines, and running, the VL increases proportionately far more than the SOL in humans (Brandell 1977, Yang & Winter 1985, Duysens et al. 1991) and cats (Smith et al. 1977, Walmsley et al. 1978). Thus, the results may simply reflect the greater capacity of the VL to respond to changes in load. Our results agree with Harkema et al. (1997), who reported a curvilinear relationship between load and SOL EMG during walking. They reported that SOL EMG amplitudes changed little for loads of 50% to 100% body weight. This may also explain the lack of change in SOL EMG amplitude with sustained unloading in this study.

Comparison of application of load vertically versus through the long axis of the leg

Collaborative work done by Dr.Yang and myself with Drs. J.E. Misiaszek and K.G. Pearson has further examined the changes in timing and activation of the muscles of the lower limb with increased load (Misiaszek, Stephens, Yang, and Pearson, 2000). In this study, load was applied through the long axis of the leg during late stance, as opposed to being directed downward as described in the vertical loading study. The application of the load was via two cables attached to a belt that fitted snugly around the hips at the level of the iliac crest. The cables were directed through pulleys that were attached to the frame of the treadmill the subjects were walking on. While the 11 subjects studied were walking on the treadmill, one experimenter would pull on the cables, with the force being applied monitored by a force transducer that was mounted in series with the cables, while the limb of interest was extended during late stance. At this moment in the step cycle, the foot was located on the treadmill just ahead of the pulleys, so that the force was administered along the long axis of the leg. The force applied was approximately 60% of the subject's body weight and the force pulse lasted approximately 500 ms. Electromyography of the TA, Soleus, VL and BF were recorded. In addition, the step cycle timing was calculated in 8 of the 11 subjects from the recording of the ankle goniometer, which showed a sharp dorsiflexion at toe-off and a sharp increase in plantarflexion at heel strike.

The initial results of this study showed more drastic differences than those of the study where the application of the load was vertical through the Cof M. This means of applying load resulted in co-contraction of the extensors and the flexors of the ankle (at approximately 60 ms) and the knee (at approximately 110-120 ms). The EMG bursts of the muscles were significantly increased in magnitude of activation and prolonged compared to those seen during normal walking. An earlier onset of TA and VL activity was seen from that seen during normal walking. As well, there was significant prolongation of the step cycle and stance phase durations with the application of load (75.1ms increase in stance phase duration).

Why were such differences in the effects due to loading seen between the two experiments. One possible explanation could be due to the different postural requirements with the different means of loading. In the study where load was added along the long axis of the leg during late stance, the force applied had both horizontal backward component and vertical downward component. This is different than that where load is applied directly downward through the Cof M, where the force would mainly consist of a large vertical component, with no or very small horizontal forces occurring. The horizontal component of the force would result in a backwards movement of the CofM, which would have to be compensated by a corrective postural reaction. To remove as much as possible of the confounding postural component seen with loading along the long axis of the limb, an additional condition was added to this experiment. Here, the same test was repeated, except that while walking, the subject held a fixed railing situated in front of them. From a rough estimation of the CofM movement using video analysis of one subject, it appeared that the CofM was displaced backwards approximately ½ the distance during the trials where the rail was held as opposed to those where it wasn't. Monitoring of the vertical ground reaction force in 4 of the 11 subjects studied, via a Kistler Gaitway treadmill equipped with force plates beneath the treadmill belt, showed that the vertical loading on the leg was very similar in both conditions (351.1 N in the unsupported condition compared to 399.4 N for the supported condition).

With the backwards displacement and the subsequent corrective postural adjustments reduced, the effects of the loading appeared similar to those found in the study described in this chapter. While there was an increase in the magnitude of activation of the Soleus muscle, the co-contraction of TA was not seen, and it was not activated earlier than that seen in normal walking. As well, there was not a consistent response seen in the VL and BF, much as these muscles did not have consistent responses in the vertical loading paradigm. There did not appear to be a major prolongation of activity in the Soleus or the duration of the step cycle, and the stance phase was only increased by 12.9 ms.

The implication of these studies appears to be that in normal adult human walking, application of load results in changes in the magnitude of the extensor activity, but no significant effects on the timing of the step cycle. However, when postural instability is added with the increase in load, there are subsequent changes in timing required to help compensate for the postural disturbance and maintain the walking pattern.

Differences between preparations

Different preparations of the cat respond differently to load. Activation of afferents from extensor muscles causes strong effects in the immobilized decerebrate cat (Gossard et al. 1994), weaker effects in the walking decerebrate cat (Whelan et al. 1995), and much weaker and more variable effects in the intact cat (Whelan and Pearson 1997). A similar reduction in the response to stimuli delivered to cutaneous or mixed nerves of the foot is seen in premammillary compared with intact cats (compare Duysens & Pearson 1976 with Duysens & Stein 1978). In the present experiment, intact, adult subjects knew the experimental protocol, and knew that the loads were not threatening to their walking. Under these conditions, it is possible that input from higher centres modifies the strength of appropriate reflexes, producing just enough response to compensate for the load. In contrast, infants may be unable to influence the response of lower centres to the disturbance, because of the immaturity of descending input from the brain.

The ability of any single sensory signal to affect the walking rhythm may depend on the presence and strength of other rhythmic input. Most of the studies on load sensitive afferents in cats used a train of electrical pulses to a muscle or cutaneous nerve, a very synchronous input. Moreover, the nerve was cut before applying the stimulation, to avoid confounding problems with eliciting a direct motor response (Conway et al. 1987; Pearson & Collins 1993). In the extreme case, the animals were paralysed, totally removing rhythmic sensory input (Conway et al. 1987; Gossard et al. 1994; Guertin et al. 1995). Under these conditions, activation of any afferent is likely to produce a large effect, since it is acting against a background of relative electrical silence. With increasing presence of other rhythmic input, such as in the walking decerebrate cat with minimal denervation (Whelan & Pearson 1997), the effects are reduced.

The study with decerebrate cats which most closely mimics the mechanical loading used here with humans, is one in which the walking decerebrate cat was suddenly either lifted or lowered (Hiebert 1996), resulting in a doubling or halving of the patellar force. His results were similar to ours: changes in the EMG amplitude of the quadriceps muscle, but rather little change in the SOL and little change in the duration of the stance phase and step cycle. Orlovsky (1972) increased load on the limbs by raising the whole treadmill that decerebrate cats were walking on, while the cats were fixed to a frame. This increased the magnitude of the extensor EMGs, but did not change the burst duration. Load on the extensor muscles is also increased when walking up an incline. Intact cats walking up an incline did not modify the stance phase and cycle durations, but did increase the amplitude of the extensor EMGs (Carlson-Kuhta et al. 1998). Together, these data indicate that the more intact the cat, the smaller the changes in stance phase and cycle duration. Extensor EMG amplitudes, however, always seemed to change with load. Perhaps when competing rhythmic input from other afferents and descending pathways are present, the ability of any single input to entrain the rhythm is much reduced.

Conclusions

Transitions between stance and swing phases of walking are critical to the maintenance of balance in a biped. Perhaps for this reason, the control of transitions between phases relies more heavily on supraspinal structures in the human. Whatever the mechanism, the control of the amplitude and duration of the response can be independently varied in the adult. Presumably, this provides greater flexibility for responding to changes in load under different conditions.

3.5 REFERENCES

Brandell B.R., 1977. Functional roles of the calf and vastus muscles in locomotion. *Am. J. Physiol. Med. 56*:59-72.

Carlson-Kuhta P., Trank T., Smith J.L., 1998. Forms of forward quadrupedal locomotion. II. a comparison of posture, hindlimb kinematics, and motor patterns for upslope and level walking. *J. Neurophysiol. 79*:1687-1701.

Conway B.A., Hultborn H., Kiehn O., 1987 Proprioceptive input resets central locomotor rhythm in the spinal cat. *Exp. Brain Res. 68*:643-656.

Duysens J., Pearson K.G., 1976. The role of cutaneous afferents from the distal hindlimb in the regulation of the step cycle of thalamic cats. *Exp. Brain Res. 24*: 245-255.

Duysens J., Pearson, K.G., 1980. Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Res. 187*: 321-332.

Duysens J., Stein R.B., 1978. Reflexes induced by nerve stimulation in walking cats with implanted cuff electrodes. *Exp. Brain Res. 32(2)*: 213-224.

Duysens J., Tax A.A.M., van der Doelen B., Trippel M., Dietz V., 1991. Selective activation of human soleus or gastrocnemius in reflex responses during walking and running. *Exp. Brain Res. 87*:193-204.

Edgerton V.R., Smith J.L., Simpson D.R., 1975. Muscle fibre type populations of human leg muscles. *Histochem. J. 7*:259-266.

Eke-Okoro S.T., Larsson L.-E., 1984. A comparison of the gaits of paretic patients with the gaits of control subjects carrying a load. *Scand. J. Rehab. Med. 16*: 151-158.

Finch L., Barbeau H., Arsenault B., 1991. Influence of body weight support on normal human gait: development of a gait retraining strategy. *Phys. Ther. 71*:842-856.

Fouad K., Pearson K.G., 1997. Effects of extensor muscle afferents on the timing of the locomotor activity during walking in adult rats. *Brain Res. 749(2)*: 320-328.

Ghori G.M.U., Luckwill R.G., 1985. Responses of the lower limb to load carrying in walking man. *Eur. J. Appl. Physiol. 54*:145-150.

Gossard J.-P., Brownstone R.M., Barajon I., Hultborn H., 1994. Transmission in a locomotor-related group Ib pathway from hindlimb extensor muscles in the cat. *Exp. Brain Res. 98*: 213-228.

Guertin P., Angel M.J., Perreault M.C., McCrea D.A., 1995. Ankle extensor group I afferents excite extensors throughout the hindlimb during fictive locomotion in the cat. *J. Physiol. 487*:197-209.

Harkema S.J., Hurley S.L., Patel U.K., Requejo P.S., Dobkin B.H., Edgerton V.R., 1997. Human lumbosacral spinal cord interprets loading during stepping. *J. Neurophysiol. 77*:797-811.

Hiebert G.W., 1996. *Afferent Regulation of Phase Transitions and Muscle Activity during Walking in the Cat.* PhD Thesis, University of Alberta.

Iizuka M., Kiehn O., Kudo N., 1997. Development of neonatal rats of the sensory resetting of the locomotor rhythm induced by NMDA and 5-HT. *Exp. Brain Res. 114*:193-204.

Johansson R.S., Westling G., 1987. Signals in tactile afferents from the fingers eliciting adaptive motor responses during precision grip. *Exp. Brain Res. 66*:141-154.

Johnson M.A., Polgar J., Weightman D., Appleton D., 1973. Data on the distribution of fibre types in thirty-six human muscles. An autopsy study. *J. Neurol. Sci. 18*:111-129.

Misiaszek J., Stephens M.J., Yang J.F., Pearson K.G., 2000. Early corrective responses of the leg to perturbations at the torso during walking in humans. *Exp. Brain Res. 131*(4): 511-523.

Nilsson J., Thorstensson A., 1987. Adaptability in frequency and amplitude of leg movements during human locomotion at different speeds. *Acta Physiol. Scand. 129*:107-114.

Orlovsky G.N., 1972. The effect of different descending systems on flexor and extensor activity during locomotion. *Brain Res. 40*:359-371.

Pearson K.G., Collins D.F., 1993. Reversal of the influence of group Ib afferents from plantaris on activity in medial gastrocnemius muscle during locomotor activity. *J. Neurophysiol. 70*:1009-1017.

Pearson K.G., Ramirez J.M., Jian W., 1992. Entrainment of the locomotor rhythm by group Ib afferents from ankle extensor muscles in spinal cats. *Exp. Brain Res. 90*:557-566.

Simonsen E.B., Dyhre-Poulsen P., Voigt M., Aagaard P., Sjøgaard G., Bojsen-Møller F., 1995. Bone-on-bone forces during loaded and unloaded walking. *Acta Anta. 152*:133-142.

Smith J.L., Edgerton V.R., Betts B., Collatos T.C., 1977. EMG of slow and fast ankle extensors of cat during posture, locomotion and jumping. *J. Neurophysiol. 40*:503-513.

Stephens M.J., Yang J.F., 1996a. Short latency, non-reciprocal group I inhibition is reduced during the stance phase of walking in humans. *Brain Res. 743*:24-31.

Stephens M.J., Yang J.F., 1996b. The effects of load on the human step cycle. *Soc. Neurosci. Abstr.*, p.1849.

Walmsley B., Hodgson J.A., Burke R.E., 1978. Forces produced by medial gastrocnemius and soleus muscles during locomotion in freely moving cats. *J. Neurophysiol. 41*:1203-1216.

Whelan P.J., Pearson K.G., 1997. Comparison of the effects of stimulating extensor group I afferents on cycle period during walking in conscious and decerebrate cats. *Exp. Brain Res. 117*:444-452.

Whelan P.J., Hiebert G.W., Pearson K.G., 1995. Stimulation of the group I extensor afferents prolongs the stance phase in walking cats. *Exp. Brain Res. 103*:20-30.

Yang J.F., Stephens M.J., Vishram R., 1998. Transient disturbances to one limb produce coordinated, bilateral responses during infant stepping. *J. Neurophysiol. 79*:2329-2337.

Yang J.F., Winter D.A., 1985. Surface EMG profiles during different walking cadences in humans. *EEG Clin. Neurophysiol. 60*:485-491.

Zehr E.P., Stein R.B., Komiyama T., Kenwell Z., 1995. Linearization of force sensing resistors (FSR's) for force measurement during gait. *Proc. 17th Ann. International Conf. IEEE Engineering in Medicine and Biology Soc.*, pp.300-301.

4.0 THE EFFECT OF TRANSIENT MECHANICAL LOADING ON INFANT STEPPING*

4.1 INTRODUCTION

Transient disturbances have been shown to generate specific, repeatable responses in the walking human (reviewed in Dietz, 1986; Stein, Yang, Edamura and Capaday, 1991). The responses found in the human qualitatively resemble those found in other mammals such as the cat (reviewed in Rossignol, 1996), but quantitative differences exist. One example is the effect of loading on the stance-to-swing transition. In reduced animal preparations, unloading the extensor muscles of the limb in late stance is necessary before swing can be initiated (Duysens and Pearson, 1980; Conway, Hultborn and Kiehn, 1987; Gossard, Brownstone, Barajon and Hultborn, 1994). In the intact human, the effect of load is much weaker. Most experiments on humans have been on intact individuals (Chapters 2 and 3), whereas most experiments on cats have been on decerebrate or spinal preparations (Duysens and Pearson, 1980; Conway et al., 1987; Pearson and Collins, 1993; Gossard et al., 1994). Are these differences, observed between the cat and the human, due to differences in the underlying mechanisms that generate walking in different species or due to differences in the preparations being used.

---

* These results have been published in: Yang, J.F., Stephens, M.J. and Vishram, R. (1998a). Infant stepping: a method to study the sensory control of human walking. J. Physiol. (Lond.) 507: 927-937 and Yang J.F., Stephens, M.J. and Vishram, R. (1998b). Transient disturbances to one limb produce coordinated, bilateral responses during infant stepping. J. Neurophysiol. 79: 2329-2337. Contribution to paper: Involved with some of the data collection, data analysis associated with disturbances that caused a change in load and development of the figures.

There is some evidence that the type of preparation might be important. The response of load-sensitive receptors in the muscle show different responses depending on whether the animal is spinalized, decerebrated (McCrea, Shefchyk, Stephens and Pearson, 1995) or intact (Whelan and Pearson, 1997). The reflex responses to force changes are quite strong in immobilized spinal or decerebrate cats (Conway et al, 1987; Gossard et al., 1994; Guertin, Angel, Perreault and McCrea, 1995), less so in walking decerebrate cats (Whelan, Hiebert and Pearson, 1995) and weakest in intact cats (Whelan and Pearson, 1997). The importance of equivalent states of the human system is much more difficult to address. The only suggestion that load may have a strong effect on the spinal circuitry of walking in humans is the success of manipulating load during the retraining of walking after spinal cord injury (Harkema, Hurley, Patel, Requejo, Dobkin and Edgerton, 1997). Adult humans with either a complete spinal cord injury or a stroke to the brain stem may be in a similar state as a spinalized or decerebrated animal. However, stepping behaviour under these conditions is very rare (Calancie, Needham-Shropshire, Jacobs, Willer, Zych and Green, 1994; Hanna and Frank, 1995; Dietz, Colombo, Jensen and Baumgartner, 1995).

It would be advantageous to be able to examine a system in the human that is more comparable to the decerebrate or spinal cat. We reasoned that infants might be an alternative for such a model. Descending motor pathways from the brain to the spinal cord are not completely functional in the young infant, as revealed by the lack of response when the muscle was quiescent to transcranial magnetic stimulation (Eyre et al 1991; Muller et al., 1991). A response was generated in the muscle with transcranial magnetic stimulation when the muscle was active, though the stimulation needed to elicit a response had a much higher threshold in the infants than that required in adults (Eyre et al., 1991). In fact, the stimulus threshold value (the intensity of stimulation needed to elicit a response in the muscle 50% of the time) would remain extremely high until approximately 2 years of age. After that, it would decrease in an exponential fashion until 16 years of age, when the adult threshold value was generally attained. Morphological studies also indicate that myelination is incomplete in the corticospinal tract at this time (Yakovlev and Lecours, 1967). Infants exhibit a stepping response at birth (Peiper, 1929). A similar stepping response has been reported in anacephalic infants (Peiper, 1961), further supporting the idea that infant stepping is controlled by brainstem/spinal circuitry.

Evidence indicates that sensory input is used to regulate the stepping patterns in infants. Co-ordination of the lower limbs remains unaltered even when separate treadmill belts, running at different speeds, drive each limb (Thelen et al. 1987), similar to that seen in adults (Dietz et al. 1994). We showed recently (Yang et al., 1998a) that infants will adjust their step cycle to compensate for changes in speed, much as adults do (Grillner et al., 1979)

Since adult humans and decerebrate cats respond differently to changes in load during the stance phase, it is a logical first step to see how infants respond to this type of sensory information. If the infants respond in a similar way to the reduced cat preparations, it would be indirect evidence to show that the mechanisms used to generate stepping may be similar between the cat and the immature human.

This chapter reports both the stepping pattern of infants and their responses to transient loading during walking. The infants were all under 10 months of age. Normal stepping was elicited by holding the infants over the treadmill. The first study established that consistent stepping could be obtained in infants of all ages. The second study examined how infants responded to transient disturbances. Two types of disturbances that induced changes in load in the stance limb were used. First, motion of one limb was suddenly halted during the swing phase, and the response in the contralateral stance limb examined. Second, transient loads were applied during the stance phase, to determine how adding more load affected the overall step cycle. Both of these disturbances led to a prolongation of the stance phase and a delay in the onset of the swing phase in infants.

4.2 MATERIALS AND METHODS

Subjects

Study 1:

Thirty-eight infants who showed at least four consecutive steps on the treadmill were studied. A number of issues were addressed in the original report. Only the undisturbed stepping pattern will be considered here.

Study 2:

For the transient disturbances, twenty-one infants were studied. None could walk independently. Twelve were studied during disturbances applied in the swing phase and 12 during loading in the stance phase. Three were studied during both types of disturbances. The infants ranged in age from 3 to 10 months (mean±SD = 7.2±1.9 months). For both studies, infants were recruited through the maternity wards of hospitals, and the public health division of Capital Health in Edmonton. Ethical approval was obtained from the appropriate facilities. A parent provided informed, written consent for the infant to participate in the study. Only healthy babies, born at or after 32 weeks gestation were included.

Recording procedures

Study 1:

Beckman type surface electromyographic (EMG) electrodes were placed over 4 muscle groups in the lower limbs in either of the following combinations: quadriceps (quads) and tibialis anterior (TA) of both limbs, gastrocnemius-soleus (GS) and TA of both limbs, or quads, hamstrings, GS and TA of the left limb. Generally, miniature electrodes (2 mm recording diameter) were used for the lower leg and regular electrodes (7 mm recording diameter) were used for the thigh muscles, except for the very young infants, in which miniature electrodes were used on all muscles. The skin was cleaned with rubbing alcohol before application of electrodes. The electrode pairs were separated by approximately 1 cm.

Adhesive skin markers were placed over the superior border of the iliac spine, the greater trochanter, the knee line, the lateral malleolus and the head of the fifth metatarsal of the left lower limb. Force sensitive resistors (FSRs) (Interlink Electronics, Camarillo, CA, USA) 2.5 cm in diameter were used to indicate foot contact during stepping in experiments performed on a regular treadmill. One or two FSRs were taped to the sole of the foot or shoe, depending on the size of the infant's foot, and the footwear they normally preferred. A twin-axis electrogoniometer (Penny and Giles, Biometrics Ltd., Blackwood Gwent, U.K.) was placed over the right hip joint, because the motion of the right hip was obscured on video.

When the infants were fully instrumented, they were held over a slowly moving treadmill belt with their feet making contact with the belt. The treadmill belt speed was adjusted to a level that seemed optimal for eliciting stepping movements. A video camera recorded the motion of the left side of the body. EMG, force sensitive resistors or force platform, and electrogoniometer signals were recorded on VHS tape with a pulse code modulation (PCM) encoder (A.R. Vetter Co. Inc., Rebersburg, PA). The video and analog signals were synchronized by a digital counter that incremented light emitting diode numbers visible to the video, while at the same time sending corresponding pulses to analog tape (rate of 1 Hz).

Study 2:

The same recording procedures as outlined in Study 1 also apply to Study 2. All subjects were weighed on an infant scale or on the force platform, depending on where the experiment was performed (ie. laboratory with or without Gaitway treadmill system, see below).

Halting the motion of the swing limb:

Once good sustained stepping was obtained, disturbances were randomly applied by hand to the right lower extremity. The right limb was stopped momentarily during its flight, either in the first or second half of the swing phase. The duration of this disturbance was varied between 0.1 to 1.7 s. The duration was estimated from the video record, with an accuracy of 33 ms.

The initial results indicated that the response of the contralateral limb was dependent on the amount of weight support on that limb at the time of the disturbance. Thus, in some infants, the disturbance was applied while the infant was bearing different amounts of weight. The amount of weight borne was controlled by the experimenter who was holding the infant. For example, at the time of the disturbance, or shortly before, the experimenter holding the infant would lift the infant to decrease the amount of load on the feet. In some trials, this resulted in airstepping. In a few trials, the disturbance duration was prolonged to (> 2 s) to determine the effect of a long disturbance.

Loading the Stance Limb:

Trials were also performed in which the limb was not disturbed during the swing phase, but additional load was applied instead during the stance phase, to examine the effect of load alone. Sudden loading was applied by having the infant bear more of her/his own weight, as controlled by the experimenter supporting the infant, or by another experimenter pushing down transiently on the pelvis. Loads were always applied transiently during the stance phase of one step. The amount of load added could not be controlled exactly. Since the FSRs only provided qualitative information about loading, 5 subjects were studied in another laboratory, where a Gaitway treadmill system (Kistler Instr. Corp., Amherst, NY) with a force platform embedded under the treadmill belt, was available (courtesy of Dr. Brian Andrews). In these experiments, the exact amount of force could be estimated. FSRs were not used in these experiments, because the force platform provided information on foot contact.

Data analysis

The video data were examined for sequences of sustained stepping. A hard copy of the raw data was printed on a chart recorder, and the sequences of data corresponding to good stepping (as identified on the video record) were selected for analysis. The EMG data were then full-wave rectified and low-pass filtered at 30 Hz, converted from analog to digital form together with the data from the force sensitive resistors, goniometer and synchronization pulse at 250 Hz (Axotape, Axon Instr. Inc., Foster City, CA). Data from both studies were processed in this way. Analyses unique to each study are described below.

Study 1:

The data from undisturbed walking steps were averaged with alignment either to: 1) the beginning of foot-floor contact, as indicated by the force sensitive resistors, or 2) the onset of muscle activity in a muscle that showed a clear bursting pattern with each step (usually the TA). The duration of the step cycle and EMG bursts were calculated from these averages.

Co-contraction was calculated from the EMG in the step cycle after averaging across a number of undisturbed walking steps. The step cycles were all normalized to 100% in time before averaging, so that slight differences in step cycle duration did not result in blurring of the EMG. The area under the averaged EMG-time curve for one muscle in a step cycle was calculated after removal of a bias. The bias was defined as a 50-100 ms window with the lowest EMG amplitude in the average. The bias values were similar to the values obtained during times when the muscle was quiescent in the same subject, as recorded during the period of quiet sitting or lying. The area under the averaged EMG from a muscle was defined as 100%, and the amplitude at each point in time expressed as a percentage of this total. The index of co-contraction was defined as the overlap in area between any two muscle pairs. For example, at any point in time in the step cycle, if both EMG's from a pair of antagonist muscles was not zero, then the overlap at that point in time was defined by the EMG with the lower amplitude. The total amount of overlap in the step cycle is the sum of these individual overlap points. The maximum possible overlap was 100%. These co-contraction indices were compared with data obtained in adults from another study (Chapter 4). The differences in the co-contraction index between infants and adults were compared using Student's t-test.

Study 2:

Halting the motion of the Swing Limb:

In the initial analysis, all swing phase disturbances were included in the analysis, so long as they: 1) did not cause the infant to slip, 2) were preceded and followed by good steps, 3) did not contain disturbances that extended over more than one step cycle, 4) did not cause both limbs to leave the treadmill (i.e., not airstepping). The number of successful right limb disturbances ranged from 1 to 14 per subject (mean = 4.4, median = 4). A total of 58 disturbances fit the criteria set out above. To check if the timing of the disturbance might influence the results, further analysis was done on whether the disturbance occurred in early or late swing.

The durations of the disturbed step cycle and those immediately preceding and following it were estimated from one of the following: the onset of TA EMG, the onset of foot-contact, or the video image, whichever provided the clearest demarkation of steps. The trials were classified as either having good weight support or poor weight support on the contralateral limb. Trials in which the ball of the foot was lifted off the treadmill belt within 200 ms after the onset of the disturbances were considered to have low weight support.

Loading the Stance Limb:

Trials in which the infant was transiently loaded were analyzed in a similar way. The duration of the load was estimated from video. Response to loading was quantified by comparing the duration of the disturbed step cycle to that preceding and following it. In some trials, the stepping rhythm stopped after load was applied. These trials were analyzed separately. For the experiments carried out on the Gaitway treadmill, the force platform was calibrated with known weights. Four force-sensitive cells, one at each corner of the force platform, measured vertical force. The total force was the sum of the 4 signals. The amount of load added in each loading disturbance was estimated as follows. The average force over the stance phase was estimated for the disturbed step and the preceding undisturbed step. The difference in force between these two stance phases represented the amount of load added during the disturbance. The amplitude of the extensor EMG (either GS or quads) and their burst duration during loading was compared with that in undisturbed walking. Only subjects who showed extensor EMGs free of artifact and clear FSR signals were used. The average EMG amplitude during the stance phase was calculated by dividing the area under the rectified and smoothed EMG signal during the stance phase by the duration of the stance phase. The stance phase was defined by the FSR or force platform signal indicating foot contact with the ground. The burst duration of the extensor EMGs were also estimated visually. Both the amplitude and duration estimates from the EMG signal were analyzed using custom written programs (MATLAB, MathWorks Inc, Natick, Mass., U.S.A.).

Statistical analysis

Study 1:

A Student's t-test was used to look for significant differences in co-contraction between the infants and the adults.

Study 2:

A repeated measures ANOVA was used to compare the durations of the disturbed step with those preceeding and following the distrubance at a significance level of 0.05. Bonferroni t test was used to compare the data post-hoc. The level of significance for the post-hoc tests were adjusted to 0.017 to guard against an increase in type I errors with multiple comparisons (Myers 1979). Student's t-test was used to compare stepping in early versus late disturbances in the swing phase. Differences in the EMG amplitude and burst duration during the stance phase were compared for loaded versus normal steps using a paired t-test. All t-tests were performed at a level of 0.05.

4.3 RESULTS

EMG patterns in normal stepping

Clear alternation of flexors and extensors could be obtained during stepping from infants of all ages. Figure 4.1 illustrates different muscle groups for three different infants, aged 2, 3.3 and 7.2 months. The EMG pattern of walking averaged across a number of steps is shown on the right hand side of Figure 4.1. Note that Quad, Ham and GS muscles are co-active in the stance phase, and the TA is active in the swing phase (Figure 4.1C). EMG bursts at the beginning of the stance phase were seen in some infants (Figure 4.1B & 4.1C). These early bursts were most commonly seen in extensor muscles, but occasionally in flexor muscles too.

The index of co-contraction averaged across all subjects who showed good EMG recordings from these muscle pairs is shown in Figure 4.2. The average index of co-contraction for the TA-Quad pair was not significantly different from adults, whereas that for the TA-GS pair was significantly higher in the infants. For an intuitive understanding of the co-contraction index, note that for the subjects shown in Figure 4.1, the average co-contraction index for the TA-Quad muscle pair was 47% for Figure 4.1A, 31% for Figure 4.1B, and 24% for Figure 4.1C.

Halting the motion of the swing limb

When the right limb was suddenly stopped during the middle of the swing phase, the rhythm in the contralateral limb was altered. Figure 4.3 shows stick figures of the contralateral (left) limb during the step preceding the disturbance, and the disturbed step. The most extended position achieved in each step is shown in the line drawing to the right.

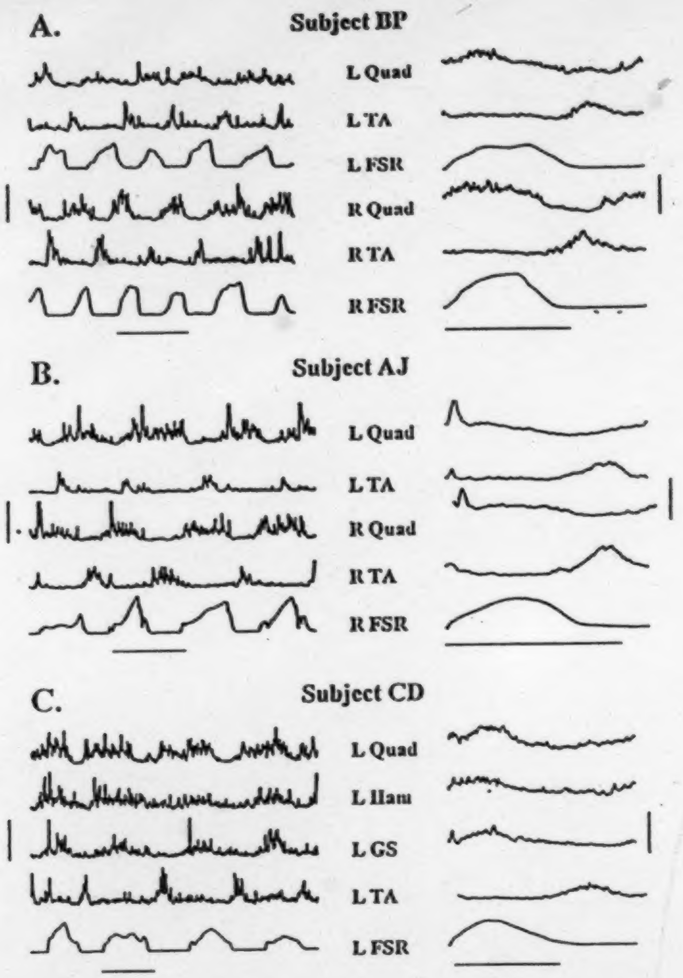

Figure 4.1. The EMGs from left and right limbs during treadmill stepping are shown for subjects BP and AJ in **A** and **B**, while those from 4 muscles in the left limb are shown for subject CD in **C**. The ages of these subjects at the time of recording were 2, 7.2 and 3.3 months, and the treadmill speed was 0.10 m/s, 0.19 m/s, and 0.12 m/s respectively, for **A**, **B** and **C**. The vertical bars on the left indicate the scale for each of the EMG graphs, which is 200 μV for **A**, 120 μV for trace 4, and 100 μV for all other traces in **B**, and 60 μV for trace 2, 50 μV for trace 4, and 100 μV for traces 1 and 3 in **C**. The data from force sensors (FSR) are in arbitrary units. The traces on the right represent the averages of a number of undisturbed steps (19 and 20 steps for the left and right legs for **A**, 62 and 72 steps for the left and right legs for **B**, and 25 steps for **C**). The EMG scale is indicated by the vertical bar on the right, which is 60 μV for trace 1 and 80 μV for all other traces in **A**, 30 μV for trace 2 and 70 μV for all other traces in **B**, and 20 μV for trace 2 and 40 μV for all other traces in **C**. The horizontal bars at the bottom of each section represents 1 s for each of the graphs.

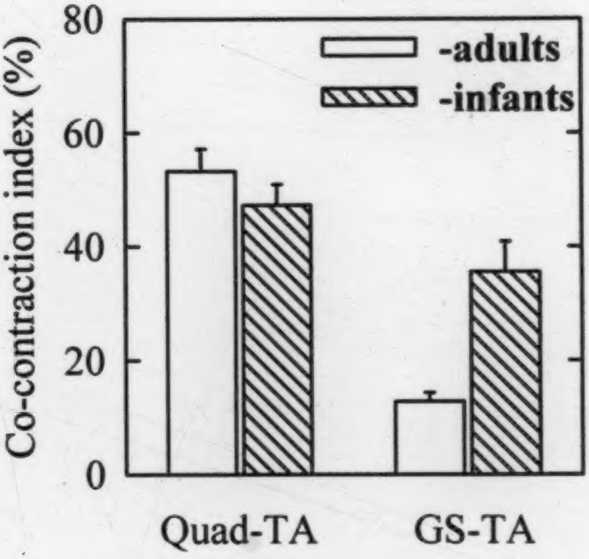

Figure 4.2. Index of co-contraction during stepping. The index of co-contraction was not significantly different for the TA-Quad muscle pair for infants and adults, but the index was significantly higher for the infants in the TA-GS pair. These data represent pooled data from 19 infants and 7 adults for the TA-Quad muscle pair, and 12 infants and 10 adults for the TA-GS muscle pair.

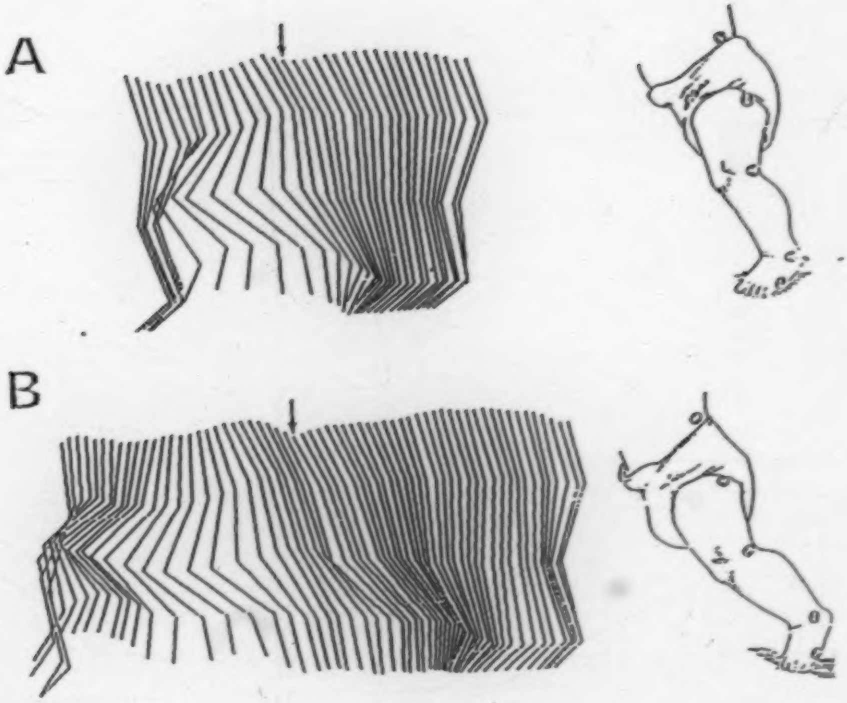

Figure 4.3. Stick figures from a step preceding (**A**) and during a disturbance (**B**) for the limb contralateral to the disturbance. The step starts from the stick figure at the far right when the foot first makes contact with the ground. Each sequential stick figure is shifted in position to the left to allow better visualization of the movement (interframe interval is 33 ms). The sequence ends at the far left with foot-floor contact. A sketch of the same limb showing the most extended position achieved in the late stance phase (corresponding stick figures indicated by arrows) is shown to the right. Note that the limb achieves greater extension during a disturbed step.

The right limb was held fixed for 500 ms during the swing phase in this disturbance. Note that the left limb reaches a much more extended position during the disturbed step. Extension occurs mostly at the metatarsophalangeal joint, but also at the hip and ankle (9° and 16°, respectively in this case). EMG activity from the same trial is shown in Figure 4.4. There was a prolongation of extensor activity (L Quad), and a delay in the onset of the flexor activity (L TA).

Another example from a different subject is shown in Figure 4.5. The FSR signals are shown for both limbs. The goniometer signal from the right hip and EMG from the left TA are also shown. The goniometer signal shows that the disturbance disrupted the motion of the swing limb. The FSRs show a prolongation of the right swing and left stance phases as a result of the disturbance.

The average prolongation of the disturbed step compared with the undisturbed step immediately preceding it was 0.497±0.21s (mean±SD). The average prolongation of the disturbed step was 0.500±0.189s for disturbances applied in the first half versus 0.541±0.363s for disturbances applied in the second half of the swing phase. Thus, the data were pooled (a total of 58 disturbances from 12 subjects).

The average cycle time of the left limb (contralateral to disturbance) for the disturbed step and those preceding and following it are shown in Figure 4.6. These were significantly different (repeated-measures ANOVA, $p<0.05$). Post-hoc tests on the individual means showed that the disturbed step was different from both the step preceding and following it, but the pre- and post-disturbance steps were not different from each other (Bonferroni t test).

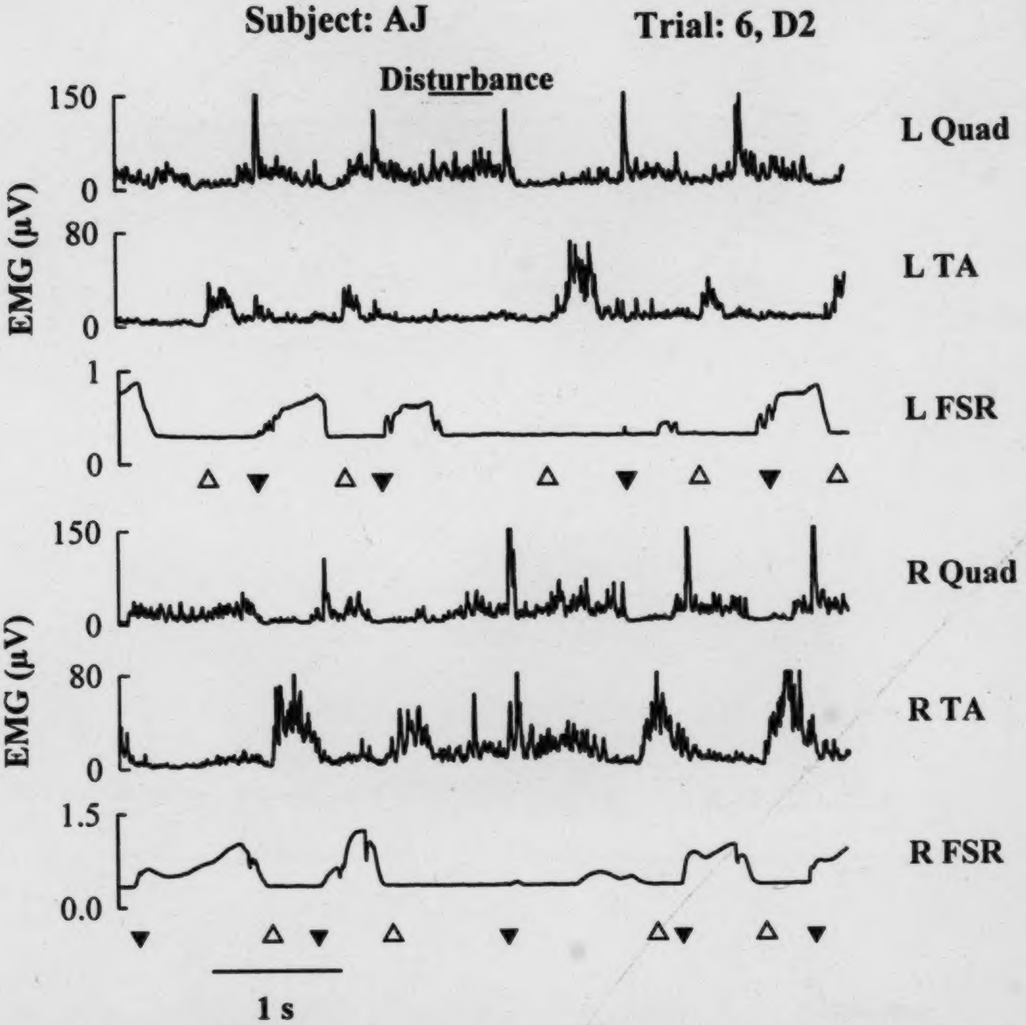

Figure 4.4. Muscle activity and foot contact pattern from the same subject as that shown in Figure 4.3, during the same disturbance of the swing limb. The rectified and smoothed EMG from a knee flexor and an ankle extensor muscle of each limb are shown for the step preceding, during and following a disturbance to the right limb. The FSR data (in arbitrary units) for each limb is shown below the corresponding EMG traces. The motion of the right limb was halted for 500 ms during the swing phase (solid line at the top of the graph). The EMG activity of the right limb is considerably altered by the disturbance. Note that the contralateral limb (left) prolonged its extensor activity, and delayed the onset of flexor activity. Note that the FSRs do not indicate the step following the disturbance clearly, so the timing of foot-contact (solid, downward triangles) and lift-off (open upward triangles) has been added. The timing was derived from the video record.

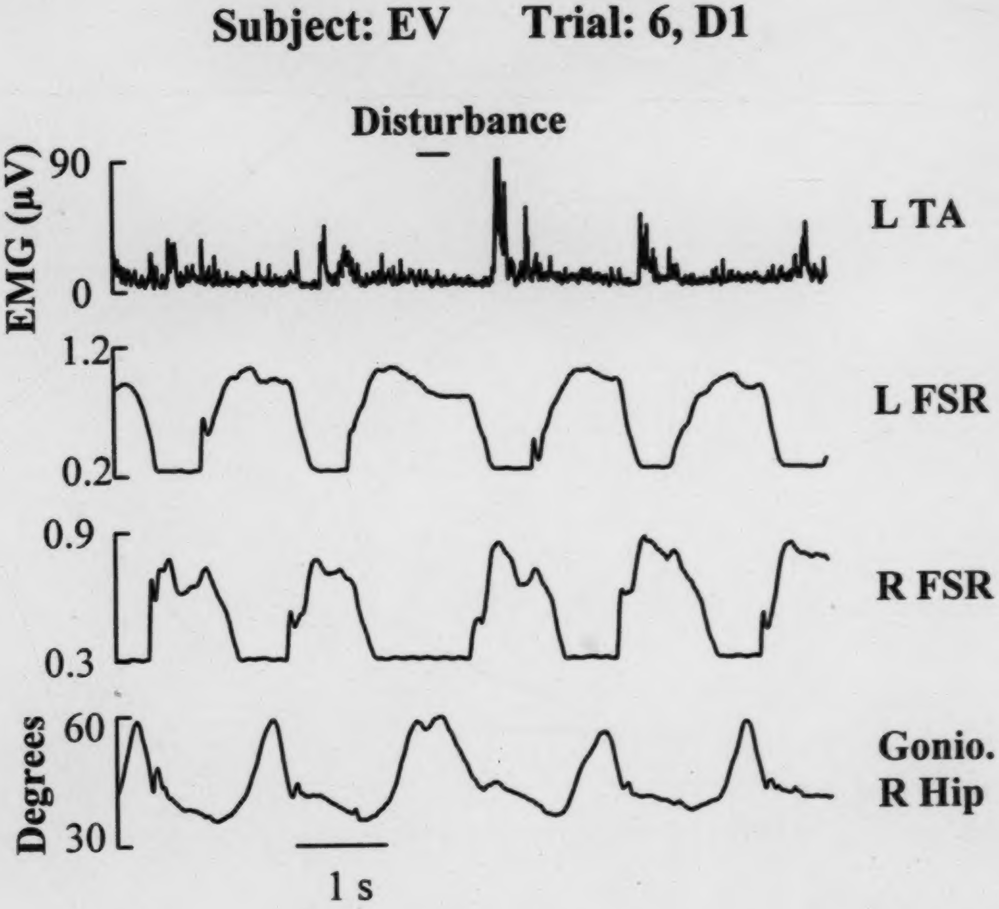

Figure 4.5. Muscle activity, foot-contact patterns, and goniometer signal from the right hip for one subject during disturbance of the swing limb (right) in stepping. Steps preceding, during and following the disturbance are shown. The signal from the force sensitive resistor (FSR) indicates foot contact with the ground when the signal is high (arbitrary units). The goniometer signal is represented in degrees, with zero degrees representing the neutral position (i.e., trunk and thigh aligned), and positive values representing flexion. Note that the hip angle never achieves the neutral position during stepping in this subject, reflecting the more flexed posture of infants. Note that during the disturbance to the right limb (duration shown by solid line at the top of the graph), the goniometer signal on the right hip shows a prolongation of the flexed position as a result of the disturbance. As in Figure 2, the stance phase is prolonged on the contralateral (left) side while the flexor activity is delayed. Note also that when the right limb resumes stepping, it does so in coordination with the left side.

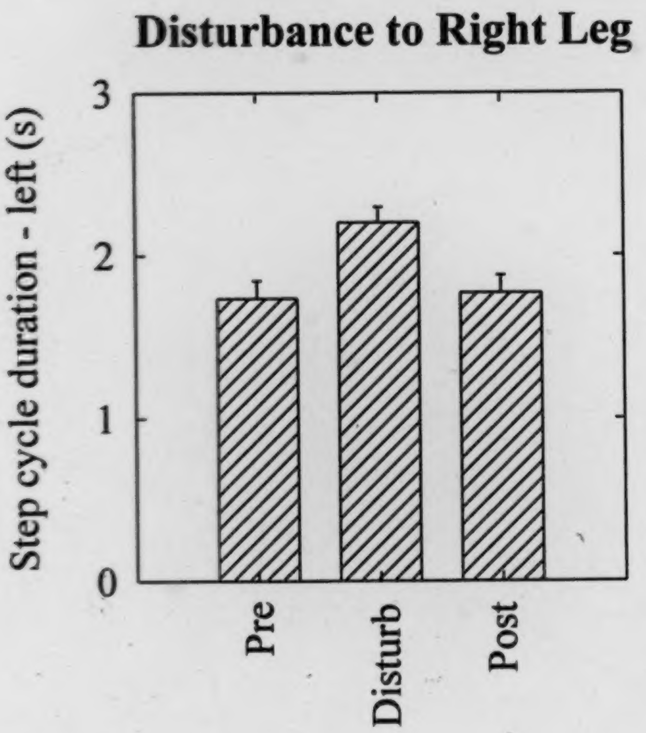

Figure 4.6. Duration of the step cycles on the left side preceding, during and following a disturbance to the right limb. The disturbances were applied during the swing phase on the right side. The averages across 12 subjects are shown with 1 standard error. The disturbed step was significantly different from the pre- and post-disturbance steps. The pre- and post-disturbance steps were not significantly different from each other.

The degree of prolongation of the stance phase in the left limb was related to the amount of weight-bearing on that limb at the time of the disturbance. In some trials, the weight on the left limb either started low or decreased during the disturbance, as the treadmill belt pulled the left limb progressively into greater extension. In such trials, left swing occurred even if the disturbance continued. An example is shown in Figure 4.7A. Of the 58 trials recorded, 4 were considered to have low weight support (i.e., weight support low at or within 200 ms of onset of the disturbance). These trials produced significantly less prolongation of the contralateral step cycle than the others (0.194±0.269 s versus 0.496±0.208 s, p,<0.05 in t-test).

In some trials, the subject bore little or no weight (i.e., airstepping). In these, stepping in the contralateral limb continued, despite the fact that the disturbance was halting stepping in the disturbed limb (Figure 4.7B). This was also observed in infants who showed good weight bearing, but were lifted up during the application of the disturbance (not shown). Note that when weight support is low, the EMGs are not as regular, and the alternation between extensor and flexor activity is less clear.

Loading of the stance limb

Transient loading during the stance phase also resulted in a prolongation of the stance phase and a delay in the onset of the swing phase (Figure 4.8). Note the prolongation of the GS EMG, and the delay in onset of the TA EMG. The FSR signals from both feet (Figure 4.8B) further show that while the left stance phase was prolonged, the right swing phase was also prolonged, so that the two limbs remained 50% out-of-phase with each other. The duration of the step cycle and the stance phase are shown for 11 of the 12 subjects in Figure

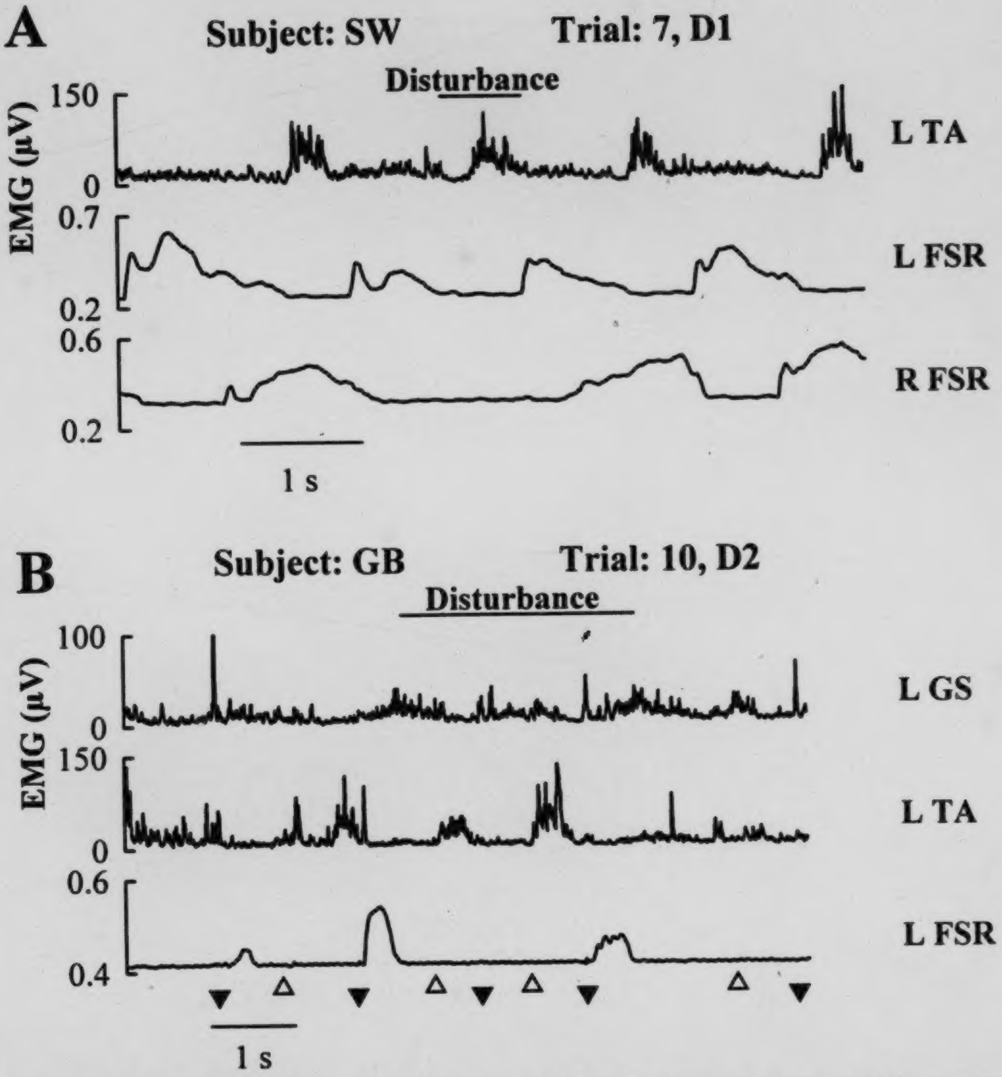

Figure 4.7. Examples from two subjects during disturbances when the weight borne on the contralateral side was very low. **A.** The disturbance was applied to the right limb, and started towards the end of the swing phase. At that time, weight support on the left was already very low (see L FSR). The disturbance did not delay the onset of the swing phase on the left side (L TA). Note also that when the right limb resumed stepping, it did so in coordination with the left side. **B.** In this subject, a prolonged disturbance to the right swing limb over 2.8 s did not prevent the left limb from continued stepping. The foot-contact and lift-off times are indicated with solid downward and open upward triangles, respectively. The FSR signal is in arbitrary units. The EMG from the gastrocnemius-soleus (GS) is not as clear when weight support is low.

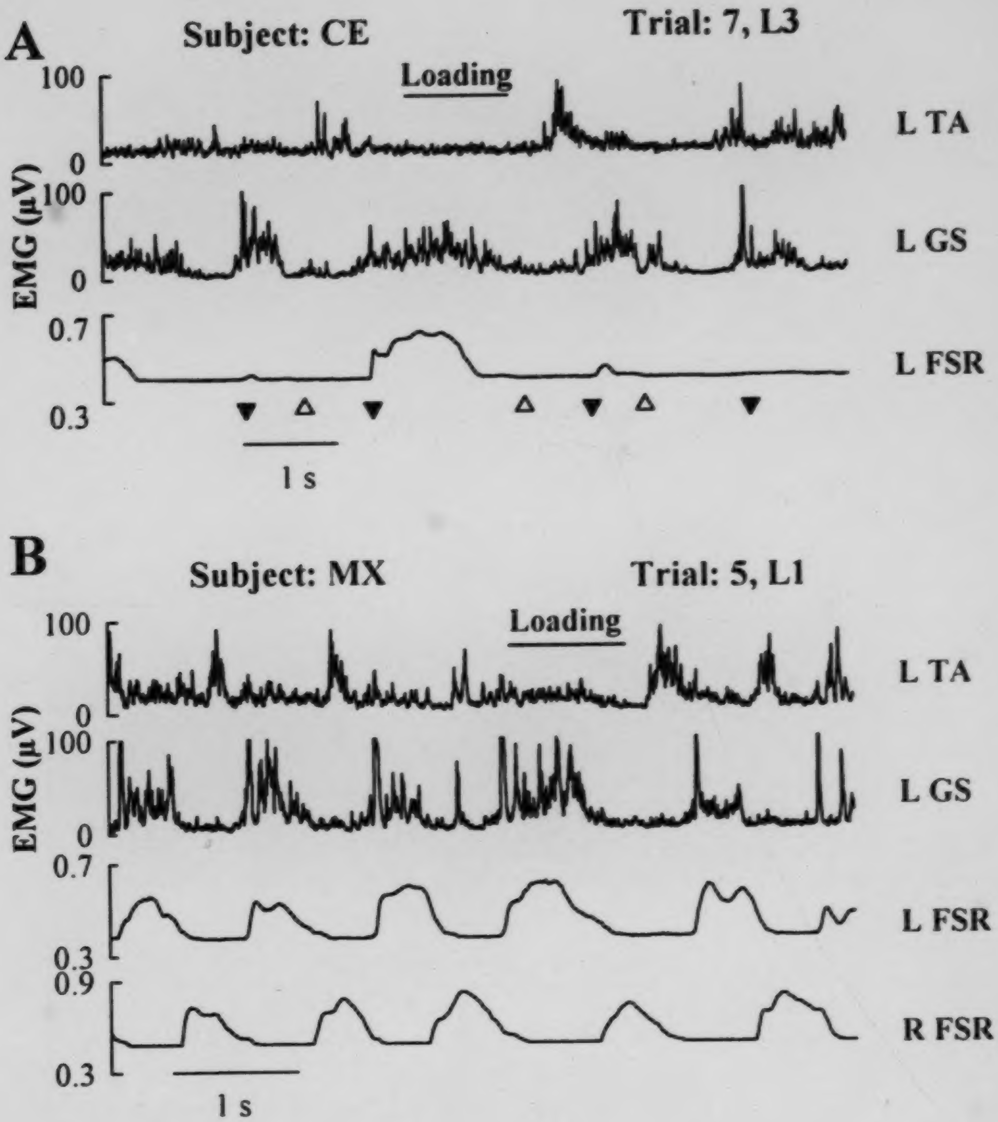

Figure 4.8. Data from two subjects, showing the response to transient loading during the stance phase. Note that during the application of load (solid line at the top of the graph), the FSR signal is larger. Moreover, the extensor activity on the loaded side is prolonged and the flexor activity is delayed. Note also that in **B**, the swing phase was prolonged on the contralateral side during the disturbance, so that the two limbs remained 50% out-of-phase with each other. The FSR signals are in arbitrary units.

4.9A. In the remaining subject, loading always stopped the stepping rhythm, so that the duration of the step with added load was very long, and there were no post disturbance steps. Both the stance phase and the cycle duration of the disturbed step were significantly prolonged compared to both the pre- and post-disturbance steps. The pre- and post-disturbance steps were not significantly different from each other (Bonferroni t test, post-hoc).

The exact amount of load added during the disturbance was estimated in 5 out of the 12 infants who stepped on a treadmill instrumented with a force platform. Figure 4.10 shows the data from one of the subjects during one of the disturbances. The average amount of load added was 22% of the infant's body weight.

The electromyographic amplitude and duration from the extensor muscles (GS or Quadriceps) was estimated in a smaller number of subjects, in whom the extensor EMGs were free of artifact. The trend was for longer burst durations during loading, and no increase in amplitude, but the differences were not significant (Figure 4.9, C and D).

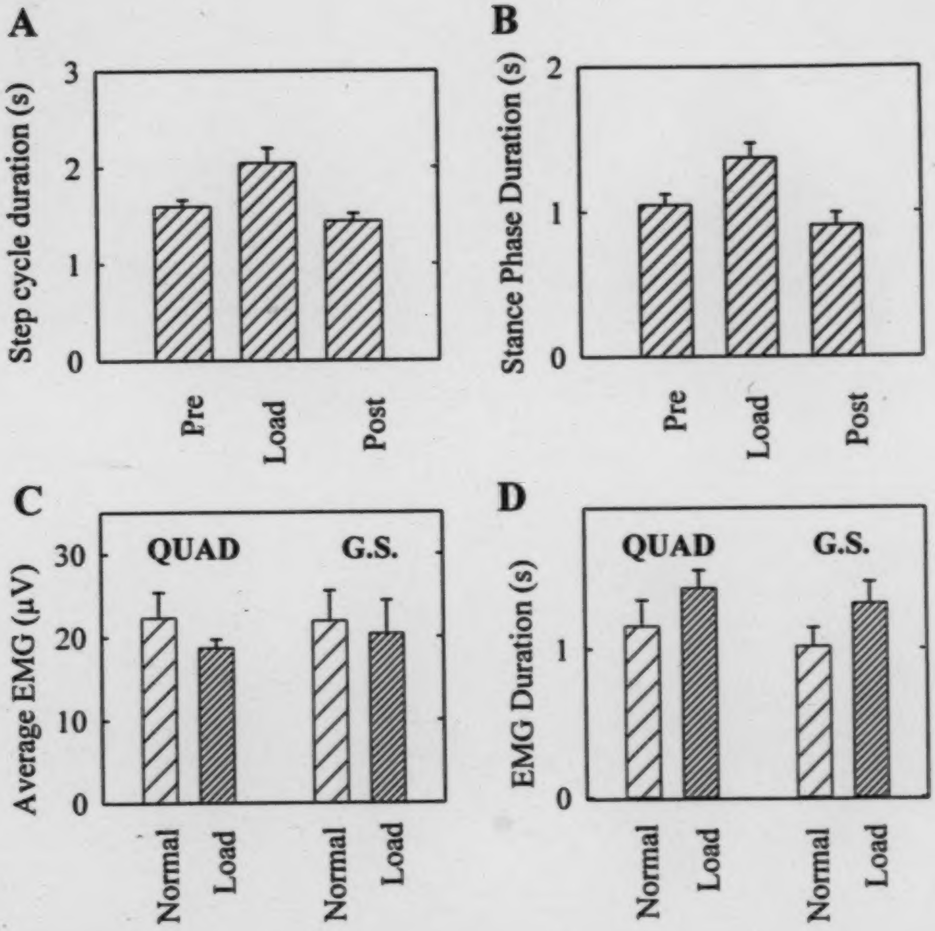

Figure 4.9. The effect of load on the duration of the step cycle (**A**), the duration of the stance phase (**B**), the amplitude (**C**) and the duration (**D**) of the extensor EMG burst. **A.** The duration of the step cycle is shown for steps preceding, during and following the application of additional load, averaged across 11 subjects (mean and 1 standard error). The step with the added load is significantly longer (28%) than the steps preceding and following it. The pre- and post-loading steps are not significantly different from each other. **B.** Most of the change in the duration of the step cycle resulted from a prolongation of the stance phase. **C.** The EMG amplitude for steps with and without extra load were averaged separately across the stance phase for each subject. The pooled data across subjects is shown here (n=4 for quadriceps and n=6 for gastrocnemius-soleus). The EMGs were not significantly different between normal steps and steps with added load. **D.** There was a trend for the EMG burst durations to be longer during loaded steps, but the difference was not significant.

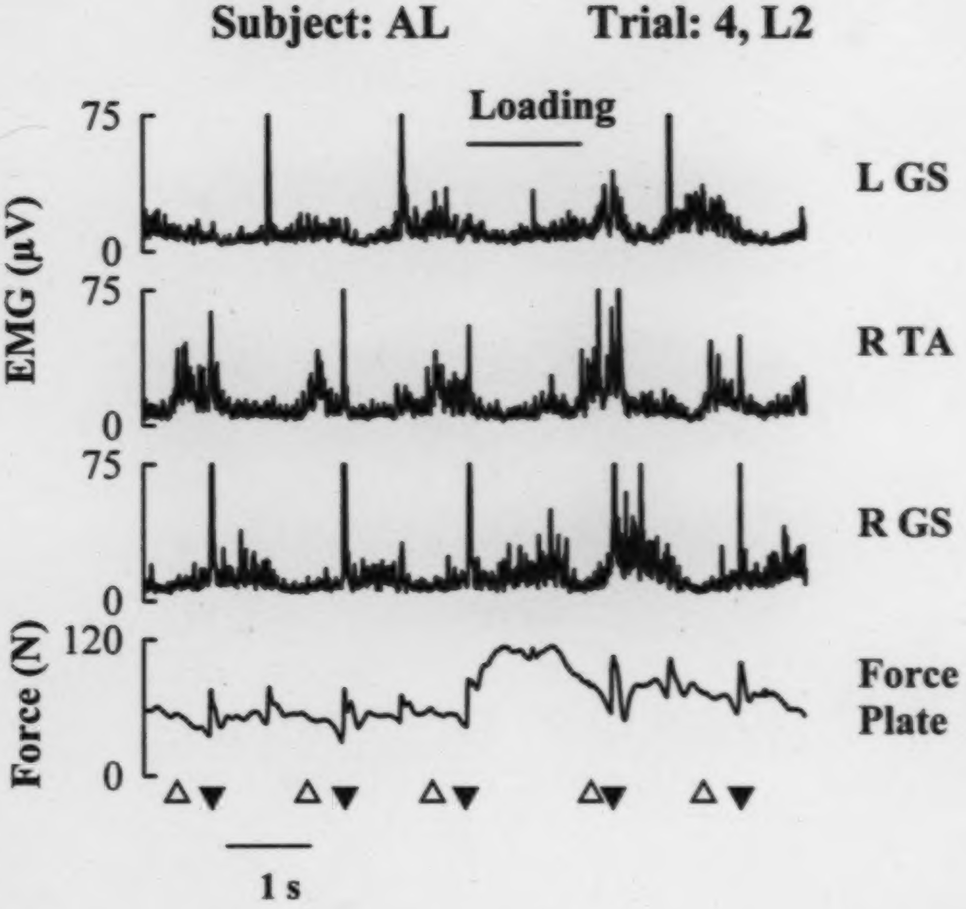

Figure 4.10. Data from a single subject during a loading disturbance applied to the right limb during the stance phase. These data were collected on the treadmill with a force platform. The EMG data are shown together with the data from the force platform. Foot-contact (solid downward triangles) and lift-off (open upward triangles) times are shown for the right foot at the bottom of the graph. Note the prolongation of extensor activity, and the delay of the onset of flexor activity. This was a trial with a particularly high loading force (48% of the subject's body weight). Note the increase in force during a disturbed step, and the clear demarkation of foot-contact in the force signal for all steps.

4.4 DISCUSSION

The data show that infant stepping is highly responsive to sensory input from the periphery. A pattern of alternation is already present at this young age, as shown by the EMG's of the flexors and extensors, though more co-contraction exists than in the adult. Transient disturbances applied to one limb in the swing phase affect the rhythm in the contralateral limb. Load added during the stance phase prolongs the duration of the step cycle. The responses to these external disturbances appear organized in a way that would facilitate equilibrium and forward progression during walking.

Characteristics of unperturbed infant stepping

Clear alternation between flexors and extensors was seen during walking in the majority of infants, in agreement with Okamoto & Goto (1985). This was true regardless of the infant's age. Since previous reports suggested co-contraction was prevalent, but did not quantify the degree of co-contraction (Forssberg, 1985; 1986; Berger et al., 1984; Thelen & Cooke, 1987; Leonard et al., 1991), we felt that such quantification would be useful. Quantification of the overlap between flexor and extensor activity indicated that larger amounts of co-contraction exist during stepping in the infant compared to the adult for the muscles about the ankle (Figure 4.2). Tonic activity of the flexors, as reported by others (Forssberg, 1985; 1986; Leonard et al., 1991), however, was rarely seen. A number of factors could account for the greater degree of co-contraction seen at the ankle in the infants. (1) The immaturity of the system. (2) Cross-talk, which remained suspect in 2 infants for the GS-TA muscle pair, and 3 infants for the Quad-TA muscle pair, as judged from the lack of independent activity between the 2 muscle groups throughout the experiment. The co-contraction index reported here, thus represents an overestimate. (3) The control of posture and equilibrium could also have lead to more co-contraction in the older infants, who supported a larger amount of their own weight, particularly in those who were held by their hands only (see also Okamoto & Kumamoto, 1972; Okamoto and Goto, 1985; Berger et al., 1984).

Independent walking requires the ability to generate rhythmic stepping movements of the lower limbs, in addition to the control of postural and volitional aspects of stepping. The stepping behaviour reported here reflects the generation of rhythmic movements primarily. This aspect of the behaviour appears well developed at birth. Indeed, the circuitry for controlling stepping is assembled very early in embryonic life. Many vertebrates including tadpoles (Stehouwer & Farel, 1985), chicks (Narayana & Hamburger, 1971; O'Donovan, Sernagor, Sholomenko, Ho, Antal & Yee, 1992) rats (Kudo, Ozaki & Yamada, 1991; Greer, Smith & Feldman, 1992; Robinson & Smotherman 1992), and cats (Graham Brown, 1915; Windle & Griffen, 1931) show spontaneous or induced locomotor movements with clear alternating flexor and extensor activity early in embryonic life (reviewed in Sillar, 1994). The ability to locomote soon after birth must have been an important evolutionary advantage in many animals. Alternating stepping-like movements are also seen very early in utero in humans, as early as 10 weeks gestation (de Vries et al., 1984). When an animal or human starts to develop the ability to walk independently, the added demands of postural control alter the muscle activation patterns initially, showing large degrees of co-contraction (Bradley & Smith, 1988; Westerga & Gramsbergen, 1993; Okamoto & Kumamoto, 1972; Okamoto & Goto, 1985; Berger et al., 1984). With practice, the co-contraction decreases, and the muscle activation pattern returns to a reciprocal pattern of firing again (Berger et al., 1984; Okamoto & Goto, 1985).

The EMG profiles from averaged data (Figure 4.1, right) indicate that some of the characteristics of adult walking are not yet present. For example, the two burst pattern in the TA muscle (one in the swing phase, and one at the transition from swing to stance), typical of adult plantigrade walking, is absent in these infants. Peculiarities of infant stepping, reported by others, were also noted. A burst of activity at the beginning of the stance phase, particularly in the GS muscle, but sometimes in other muscles as well was common in infants, in agreement with others (Forssberg, 1985; Berger et al., 1984; Leonard et al., 1991). This is likely related to the hyperactive spinal reflexes at this time in life (e.g., Mayer & Mosser, 1973; Myklebust, Gottlieb & Agarwal, 1986; Issler & Stephens, 1983).

Characteristics of the response to disturbances

Halting the motion of the swing limb causes the contralateral leg to prolong ground contact. In bipedal walking, this could prevent falling. Similar disturbances in adults produce comparable responses (Dietz et al. 1986). An intriguing aspect of our results is the importance of afferent input from the ipsilateral limb in controlling that limb during walking. For example, when the movement of the swing limb was temporarily halted, the response in the contralateral stance limb was very dependent on the conditions in the stance limb. If the weight support was high, the response was clear. If the weight support was low, the effects were muted. This indicates that load on the stance limb is very important in determining the response.

The effect of load was studied directly in the second type of disturbance. Adding load during the stance phase, whether by disturbing the contralateral limb or by pushing down on the pelvis, prolonged the duration of the stance phase and the step cycle. Removing load, whether by the treadmill pulling the leg back or by the experimenter lifting the baby, both resulted in initiation of the flexor burst and swing phase. Moreover, previous data on airstepping in the infant showed cycle durations that were much shorter than those seen in treadmill walking (data not shown). Together, these results are consistent with those reported for spinal and decerebrate cats (e.g., Duysens and Pearson 1980; Conway et al. 1987; Pearson and Collins 1993; Whelan et al. 1995; Gossard et al. 1994; Giuliani and Smith 1985). In some of these studies, loading was simulated by electrical stimulation of the muscle nerve (Whelan et al. 1995; Guertin et al. 1995; Pearson and Collins 1993; Gossard et al. 1994; Conway et al. 1987; McCrea et al. 1995; Pearson et al. 1992), or the ventral root (Duysens and Pearson 1980; Pearson et al. 1992). In other studies, muscle force was increased by direct stretch of the extensor muscles (Duysens and Pearson 1980), or transient unweighting or weighting of the hindlimbs (Hiebert 1997). In all cases, increase in load prolonged the stance phase, whereas decrease in load shortened the stance phase.

The powerful effect of loading during walking in infants is in contrast to earlier reports in adults (see Chapters 2 and 3). The results suggest that the circuitry in the spinal cord/brain stem for controlling how to respond to loads during walking is more potent in the infant than adults. With maturation, changes occur that modify how adult humans respond to load. More modest effects from activating load-sensitive afferents were also reported for the intact cat (Whelan and Pearson, 1997). Presumably, the influence of the cerebrum modifies the behaviour of the spinal/brain stem circuitry. Indeed, recordings from cells in the motor cortex in intact cats suggest that a large proportion of these cells fire at the transition from the stance to swing phase, and may play a role in this transition (Armstrong and Drew 1984; Drew 1991).

Adding load to the limb in the stance phase may have inadvertently placed the hip in a more flexed position while under load. A more flexed position of the hip may itself inhibit the initiation of swing, as suggested by work on spinal cats (Grillner and Rossignol 1978). Detailed examination of the data suggests that the effect of hip position may have been quite weak, however. As seen in Figure 4.3, under load, the hip was extended beyond the extension angle achieved in undisturbed steps, yet the flexor burst was still inhibited. Distinguishing the importance of hip position versus load on the limb will require further experiments.

Lower centres in the CNS contain details for how to respond to disturbances

Bernstein (1967) suggested that the details of movement are organized at lower levels of the nervous system, to free the higher centres of such laborious tasks. With respect to walking, considerable evidence from animal work supports his idea (e.g., reviewed in Grillner 1981; Rossignol 1996). Some data from humans also suggest that the human spinal cord may be capable of generating the rhythmic movements of walking, although the evidence is less direct (e.g., Holmes 1915; Kuhn and Macht 1948; Bussel et al. 1989; Calancie et al. 1994; Dietz et al. 1996; Dimitrijevic, Gerasimenko and Pinter, 1998). The present study provides further evidence that the circuitry for stepping is operational in infants. It is probably controlled by the lower centres in the central nervous system (Forssberg 1985). Not only do these lower centres control the details for generating the rhythmic movements, but they also contain the circuitry for responding to unexpected disturbances in an organized, useful way, like that seen in spinal cats (Forssberg et al. 1975, 1977).

Comparison between the responses in adults and infants

The maturity and sophistication of the response in these infants can be estimated by comparing them to adults faced with similar disturbances. When the right limb was unexpectedly stopped during its swing phase and prevented from progressing into stance in these infants, the contralateral limb remained in the stance phase. For bipedal walking, this is an important strategy to maintain balance. Dietz and colleagues (1986) provided a similar but much shorter disturbance (20 to 160 ms) to adults by holding the swing limb momentarily at different points during the swing phase with a cord attached to the lower leg. When the disturbance was applied early in the swing phase, the contralateral stance phase was prolonged, just as in infants.

Transient loading in the infants, in contrast, produced quantitatively different responses than those seen in adults. Our earlier work suggested that activation of load sensitive receptors in the lower limb during walking, whether by electrical stimuli to peripheral nerves (Chapter 2) or weights applied to the body (Chapter 3), has little effect on the duration of the step cycle. Transiently adding loads equivalent to 30% of the adult's body weight causes an increase in the amplitude of the extensor EMGs, but prolongs the duration of the stance phase only slightly (3%). The same load has an even smaller effect on the cycle duration (0.5%). This effect is also seen in the work of Misiaszek and colleagues (2000), where unless postural stability is compromised, there is very small effects on the timing of the step cycle or stance duration. In contrast, load experienced by the lower limbs during the stance phase of infant stepping has a very powerful effect on the duration of the step cycle (28%, see Figure 4.9), but no effect on the EMG amplitude. Based on the results obtained from the treadmill instrumented with a force platform, the loads applied to the infant were in the same range as those applied in the adult (22% of body weight for the infants and 30% body weight for the adults).

Why were the response of adults and infants similar for the disturbances applied during the swing phase, and different for loads applied during the stance phase? We think it may be explained by the participation of higher centres in the nervous system in the adult, but not in infants. When load is applied to the infant during the stance phase, the spinal/brain stem system might respond by the rule that load means the limb is not ready for the swing phase. Therefore, the stance phase is prolonged and the swing phase is delayed, just as in the decerebrate cat (e.g., Duysens and Pearson 1980). In contrast, when load was applied during the stance phase in the adult in a very controlled and consistent way, there was no real danger to the individual or to their forward progression. Thus, higher centres in the nervous system could diminish the influence of the spinal/brain stem system, increasing extensor EMG amplitude to avoid disruption of the stepping rhythm in both infants and adults. In contrast, halting the swing limb threatens equilibrium and continued forward progression. In this case, it is functionally important that the adult also modify its stepping, to ensure stability. We do not know whether the response in the adult represents the behaviour of similar spinal/brain stem circuits as in the infants, or whether supraspinal systems take over the control, and happen to generate a similar response.

The studies on adults and infants provide evidence that the timing and amplitude of the extensor EMG burst in response to load are controlled independently. Moreover, the time course of the maturation of the two responses to load is different. The control of sensory input shows rapid and dramatic changes within the first few days of life in the rat (Iizuka et al., 1997). Perhaps the response to load also changes with age in the human infant, but with a slower time course.

Conclusions

In summary, infants respond to unexpected disturbances during stepping in an organized fashion that appears to be suited for maintaining equilibrium and forward progression. All this occurs well before independent walking is possible. In this study, load is increased on the stance limb by means of either a transient increase in load directly on the stance limb or due to an interruption in the progression of the limb in swing. Regardless of how the increase in load occurs, there is a dramatic increase in the stance phase duration. This is markedly different than some findings in the intact adult human system. The responses in infants and adults is the same when a transient loading occurs due to an interruption of the progression of the swing limb will result in a prolonged stance phase. However, when transient increase in the load on the stance limb in the adult is applied directly, it results in an increase in the magnitude of the extensor EMG burst, as opposed to a significant prolongation of the stance phase. Infant responses seem to be dependent on the brain stem/spinal systems, as their responses to the different types of transient loading is very similar to that of the reduced cat preparations. This suggests that the brain stem/spinal response to load in the cat and human may be similar.

However, with functional maturity of the supraspinal connections in the adult human, responses to transient loading can be determined by the perception of how much instability to postural balance is introduced with the disturbance. This is shown by the different response elicited to the transient loading induced directly by adding weight around the CofM, which doesn't introduce much postural instability, compared to the response due to the disturbance of halting the opposite swing leg, where balance may be disturbed. Infants may not have the ability to modulate their responses to account for the "potential danger" of the disturbance encountered.

Infants appears to have one response to compensate for a change in the amount of load on the stance limb, regardless of how that increase occurs. The immature development of the connections from the supraspinal centres may not allow for differences in the perception of the potential danger from different disturbances. The infant may then just use the one standard response, dependent on brain stem and spinal systems, to compensate for all types of loading disturbances.

4.5 REFERENCES

Armstrong D.M., and Drew T., 1984. Locomotor-related neuronal discharges in cat motor cortex compared with peripheral receptive fields and evoked movements. *J. Physiol. 346*: 497-517.

Berger W., Altenmueller E., and Dietz V., 1984. Normal and impaired development of children's gait. *Human Neurobiology 3*: 163-170.

Bernstein N.A., 1967. *The Coordination and Regulation of Movements*. Pergamon, Oxford.

Bradley N.S., and Smith J.L., 1988. Neuromuscular patterns of stereotypic hindlimb behaviours in the first two postnatal month. I. Stepping in normal kittens. *Dev. Brain Res. 38*: 37-52.

Bussel B., Roby-Brami A., Yakovleff A. and Bennis N., 1989. Late flexion reflex in paraplegic patients. Evidence for a spinal stepping generator. *Brain Res. Bull. 22*: 53-56.

Calancie B., Needham-Shropshire B.N., Jacobs P., Willer K., Zych G., and Green B.A., 1994. Involuntary stepping after chronic spinal cord injury. *Brain 117*: 1143-1159

Conway B.A., Hultborn H. and Kiehn, O., 1987. Proprioceptive input resets central locomotor rhythm in the spinal cat. *Exp. Brain Res. 68*: 643-656.

De Vries J.I.P., Visser G.H.A., and Prechtl, H.F.R., 1984. Fetal motility in the first half of pregnancy. In: *Clinics in Developmental Medicine. Continuity of Neural Functions from Prenatal to Postnatal Life*, (ed.) Prechtl, H.F.R., pp. 6-64, Lavenham, Suffolk.

Dietz V., 1986. Short and long latency proprioceptive reflexes during the standing and stepping of normal and hemiparetic human subjects. In: *Neurobiology of Vertebrate Locomotion*, ed. Grillner, S., Stein, P.S.G., Stuart, D.G., Forssberg, H., Herman, R.M., Wenner-Gren International Symposium Series, Vol. 45, pp.661-671, Macmillan, London.

Dietz V., Quintern J., Boos G., and Berger, W., 1986. Obstruction of the swing phase during gait: phase-dependent bilateral leg muscle coordination. *Brain Res. 384*: 166-169.

Dietz V., Zijlstra W., and Duysens J., 1994. Human neuronal interlimb coordination during split-belt locomotion. *Exp. Brain Res. 101*: 513-520.

Dietz V., Colombo G., Jensen L., and Baumgartner L., 1996. Locomotor capacity of spinal cord in paraplegic patients. *Ann Neurol 37*: 574-582.

Dimitrijevic M.R., Gerasimenko Y. and Pinter M.M., 1998. Evidence for a spinal central pattern generator in humans. In: *Neuronal Mechanisms for Generating Locomotor Activity, Annals of the New York Academy of Sciences, Vol. 860.* (eds.) Kiehn O., Harris-Warrick R.M., Jordan L., Hultborn H. and Kudo N., New York, pp 360-376.

Drew T., 1991. Visuomotor coordination in locomotion. *Curr. Opin. Neurobiol. 1*: 652-657.

Duysens J. and Pearson K.G., 1980. Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Res. 187*: 321-332.

Eyre J.A., Miller S. and Ramesh, V., 1991. Constancy of central conduction delays during development in man: investigation of motor and somatosensory pathways. *J. Physiol. 434*: 441-452.

Forssberg H., 1985. Ontogeny of human locomotor control I. Infant stepping, supported locomotion and transition to independent locomotion. *Exp. Brain Res. 57*: 480-493.

Forssberg, H. (1986). Development and integration of human locomotor functions. In: *Development and Plasticity of the Mammalian Spinal Cord, Fida Research Series, Vol. III*, ed. Goldberger, M.E., Gorio, A. and Murray, M. Liviana, Padova, Italy. pp53-63.

Forssberg H., Grillner S., and Rossignol S., 1975. Phase dependent reflex reversal during walking in chronic spinal cats. *Brain Res. 85*: 103-107.

Forssberg H., Grillner S., and Rossignol S., 1977. Phasic gain control of reflexes from the dorsum of the paw during spinal locomotion. *Brain Res. 132*: 121-139.

Giuliani C.A., and Smith J.L., 1985. Development and characteristics of airstepping in chronic spinal cats. *J. Neurosci. 5*: 1276-1282.

Gossard J.-P., Brownstone R.M., Barajon I., and Hultborn H., 1994. Transmission in a locomotor-related group Ib pathway from hindlimb extensor muscles in the cat. *Exp. Brain Res. 98*: 213-228.

Graham Brown T., 1915. On the activities of the central nervous system of the un-born foetus of the cat: with a discussion of the question whether progression (walking etc.) is a "learnt" complex. *J. Physiol. (Lond.) 49*: 208-215.

Greer J.J., Smith J.C., and Feldman J.L., 1992. Respiratory and locomotor pattens generated in the fetal rat brain stem-spinal cord in vitro. *J. Neurophysiol. 67*: 996-999.

Grillner S., Halbertsma J., Nilsson J., and Thorstensson A., 1979. The adaptation to speed in human locomotion. *Brain Res. 165*: 177-182.

Grillner S., and Rossignol S., 1978. On the initiation of the swing phase of locomotion in chronic spinal cats. *Brain Res 146*: 269-277.

Guertin P., Angel M.J., Perreault M.-C., and McCrea D.A., 1995. Ankle extensor group I afferents excite extensors throughout the hindlimb during fictive locomotion in the cat. *J. Physiol. (Lond.) 487*: 197-209.

Hanna J.P., and Frank J.L., 1995. Automatic stepping in the pontomedullary stage of central herniation. *Neurology 45*: 985-986.

Harkema S.J., Hurley S.L., Patel U.K., Requejo P.S., Dobkin B.H. and Edgerton, V.R., 1997. Human lumbosacral spinal cord interprets loading during stepping. *J. Neurophysiol. 77*: 797-811.

Hiebert G.W., 1997. *Afferent Regulation of Phase Transitions and Muscle Activity during Walking in the Cat.* PhD thesis, University of Alberta.

Holmes G., 1915. Spinal injuries of warfare. *Brit. Med. J. 2*: 815-821.

Iizuka M., Kiehn O., Kudo N., 1997. Development of neonatal rats of the sensory resetting of the locomotor rhythm induced by NMDA and 5-HT. *Exp. Brain Res. 114*: 193-204

Issler H., and Stephens J.A., 1983. The maturation of cutaneous reflexes studied in the upper limb in man. *J. Physiol. (Lond.) 335*: 643-654.

Kudo N., Ozaki S., and Yamada T., 1991. Ontogeny of rhythmic activity in the spinal cord of the rat. In: *Neurobiological Basis of Human Locomotion.* (eds.) Shimamura, M., Grillner, S., and Edgerton, V.R. pp.3-20, Japan Scientific Societies Press, Tokyo.

Kuhn R.A., and Macht M.B., 1948. Some manifestations of reflex activity in spinal man with particular reference to the occurrence of extensor spasm. *Bull. John Hopkins Hosp. 84*: 43-75.

Leonard C.T., Hirshfeld H., and Forssberg H., 1991. The development of independent walking in children with cerebral palsy. *Dev. Med. Child Neurol. 33*: 567-577.

Mayer R.F., and Mosser R.S., 1973. Maturation of human reflexes. Studies of electrically evoked reflexes in newborns, infants and children. In: *New Developments in Electromyography and Clinical Neurophysiology, Volume 3*, ed. Desmedt, J.E., pp394-307, Karger, Basel.

McCrea D.A., Shefchyk S.J., Stephens M.J., and Pearson K.G., 1995. Disynaptic group I excitation of synergist ankle extensor motorneurones during fictive locomotion in the cat. *J. Physiol. (Lond.) 487*:527-539.

Misiaszek J.E., Stephens M.J., Yang J.F., and Pearson K.G., 2000. Early corrective reactions of the leg to perturbations at the torso during walking in humans. *Exp. Brain Res. 131*(4): 511-523.

Muller K., Homberg V., and Lenard, H.C., 1991. Magnetic stimulation of motor cortex and nerve roots in children. Maturation of cortico-motorneuronal projections. *Electroencephalography and Clin. Neurophysiol. 81*(1): 63-70.

Myklebust B.M., Gottlieb G.L., and Agarwal G.C., 1986. Stretch reflexes of the normal infant. *Dev. Med. Child Neurol. 28*: 440-449.

Narayanan C.H., and Hamburger V., 1971. Motility in chick embryos with substitution of lumbosacral by brachial and brachial by lumbosacral spinal cord segments. *J. Exp. Zoo. 178*: 415-432.

O'Donovan M., Sernagor E., Sholomenko G., Ho S., Antal M., and Yee W., 1992. Development of spinal motor networks in the chick embryo. *J. Exp. Zoo. 261*: 261-273.

Okamoto T., and Kumamoto M., 1972. Electromyographic study of the learning process of walking in infants. *Electromyography 12*: 149-158.

Okamoto T., and Goto Y., 1985. Human infant pre-independent and independent walking. In: *Primate Morphophysiology, locomotor analyses and human bipedalism*, pp.25-45, Universityof Tokyo Press, Tokyo.

Pearson K.G., and Collins D.F., 1993. Reversal of the influence of group Ib afferents from plantaris on activity in medial gastrocnemius muscle during locomotor activity. *J. Neurophysiol. 70*: 1009-1017.

Peiper A., 1929. Die schreitbewegungen der neugeborenen. *Monatsschrift fur Kinderheilkunde 45*: 444.

Peiper A., 1961. *Cerebral Function in Infancy and Childhood*. Consultants Bureau, New York.

Robinson S.R., and Smotherman W.P., 1992. Fundemental motor patterns of the mammalian fetus. *J. Neurobiol. 23*: 1574-1600.

Rossignol S., 1996. Neural control of stereotypic limb movements. In: *Handbook of Physiology, Section 12. Exercise, Regulation and Integration of Multiple Systems.* Rowell, L.B., Sheperd, J.T. (eds.), Bethesda, MD: Am. Physiol Soc., pp.173-216.

Sillar K.T., 1994. Synaptic specificity: development of locomotor rhythmicity. *Cur. Opinion Neurobiol. 4*: 101-107.

Stehouwer D.J., and Farel P.B., 1985. Development of locomotor mechanisms in the frog. *J. Neurophysiol. 53*: 1453-1466.

Stein R.B., Yang J.F., Edamura M., and Capaday C., 1991. Reflex modulation during norma and pathological human locomotion. In: *Neurobiological Basis of Human Locomotion.* (eds.) Shimamura, M., Grillner, S., and Edgerton, V.R. pp. 335-346, Japan Scientific Societies Press, Tokyo.

Thelen E., and Cooke D.W., 1987. Relationship between newborn stepping and later walking: a new interpretation. *Dev. Med. Child Neurol. 29*: 380-393.

Westerga J., and Grambergen A., 1993. Changes in the eletromyogram of two major hindlimb muscles during locomotor development in the rat. *Exp. Brain Res. 92*: 479-488.

Whelan P.J., and Pearson K.G., 1997. Comparison of the effects of stimulating extensor group I afferents on cycle period during walking in conscious and decerebrate cats. *Exp. Brain Res. 117*:444-452.

Whelan P.J., Hiebert G.W., and Pearson K.G., 1995. Stimulation of the group I extensor afferents prolongs the stance phase in walking cats. *Exp. Brain Res. 103*:20-30.

Windle W.F., and Griffen A.M., 1931. Observations on embryonic and fetal movements of the cat. *J. Comp. Neurology 52*: 149-188.

Yakovlev P.I., and Lecours A.-R., 1967. The myelogenetic cycles of regional maturation of the brain. In: *Regional Development of the Brain in Early Life*, Minkowski A. (ed.), Blackwell: Oxford, pp.3-70.

5.0 EFFECTS OF GROUP I AFFERENT INPUT ON PARKINSONIAN GAIT*

5.1 INTRODUCTION

The cardinal symptoms of Parkinson's Disease (PD) include postural and locomotor deficits. These deficits include: shuffling steps that feature a decreased stride length and slower cadence than found in normal walking (Morris, Iansek, Matyas and Summers, 1994); lack of rhythmic alternating movements in the upper limbs; a flexed posture (especially in the neck, upper limbs, hip and knees); and a "freezing" where the initiation of stepping is impaired (Pedersen, Eriksson, and Oberg, 1991). These problems can generally be broken down into two main types of deficits. First is bradykinesia (or slowness of movement), seen in the shuffling gait. The other is a specific type of akinesia (or absence of movement), which pertains to the "freezing" phenomena. Normally, walking is considered to be an automatic activity, with the pattern of stepping being generated by the Central Pattern Generator (CPG) in the spinal cord. The locomotor difficulties found in PD therefore must be due to some deficits within the spinal circuitry or from other sources that act upon the spinal circuitry. Various studies have been done examining what these deficits are and how they affect Parkinsonian gait. How spinal reflexes contribute to these gait difficulties have not been examined in detail though. The purpose of this study is to examine how the tension in the extensor muscles and the modulation of the group Ib reflex arc that uses this afferent input may be processed differently in PD than that seen in a non-neurologically impaired population. As this information may be important in regulating the step cycle, these differences may explain some of the patient population' gait difficulties.

---

* This chapter has not been published. Contribution to chapter: Involved with the development of the experimental protocol, subject scheduling, pilot testing, data collection, data and statistical analyses, drawing of figures and writing the final version of the chapter.

Few studies have investigated the problems in initiating stepping during the gait and postural problems classified as "freezing". This symptom develops in more advanced stages of the disease (Giladi, McMahon, Przedborski, Flaster, Guillory, Kostic and Fahn, 1992; Giladi, Kao and Fahn, 1997). Of 990 PD patients studied, 318 exhibited some type of freezing, or as they were termed, "motor blocks" (Giladi et al., 1992). Eighty-six percent of these 318 patients showed freezing with the initiation of gait, 45% froze during turning, and 25% demonstrated freezing when trying to walk through a narrow space. While "freezing" is generally associated with gait in parkinsonian patients, it can also be seen in the arms, during activities such as writing or brushing the teeth; in the eyelids, causing a sustained lack of blinking; and during speech (Fahn, 1995). But these examples of freezing are exhibited by only a small percentage of parkinsonian patients. Only 11% of the 318 patients studied by Giladi and colleagues (1992) had non-gait related motor blocks.

The EMG and floor reaction forces associated with freezing show significant changes from the normal gait pattern (Yanagisawa, Ueno and Takami, 1991). Even while walking, during the push-off phase of the step cycle, PD patients' ground reaction force profiles show an insufficient thrust being generated. This results in the body not being propelled as far forward as seen in non-neurologically impaired subjects, which causes a shortened stride length (Forssberg, Johnels and Steg, 1984; Yanagisawa et al., 1991).

With freezing, while an attempt is made to shift weight between the two feet, it is not accomplished, as weight tends to stay on both feet. As well, the forces generated to propel the body forward drop to almost nothing. The EMG from the muscles of both lower limbs show rapid (4-6 Hz) bursts of contraction. While some researchers suggest that a co-contraction of antagonist muscles contribute to freezing (Andrews, 1973), others find that this co-contraction is not consistently found (Yanagisawa et al, 1991). An interesting phenomenon associated with freezing is that a patient can become "unfrozen" with visual or auditory stimuli. A number of patients who freeze during locomotion will develop "tricks" using visual or auditory signals to overcome the motor block (Fahn, 1995). This "reactivation" of walking with external cues is known as "paradoxical gait".

The question that arises from these results is what prevents stepping from being initiated. To initiate a step, past research in animals and humans has shown that a requirement for the stance-to-swing transition is an unweighting of the stance limb (Duysens and Pearson, 1980). For swing to occur, a significant portion of weight must be removed from the stance limb. This is monitored by afferent signals from the periphery, and sent to the central nervous system. As the leg is unweighted, the afferent input from the load-monitoring receptors of the extensor muscles decreases. This decrease causes the extensor half-centre of the central pattern generator (CPG) to become deactivated and its inhibition of the flexor half-centre is removed. The flexor half-center becomes active and moves the limb into swing. If there is a problem with the processing of the afferent input indicating the amount of load placed on the extensor muscles in Parkinson's disease, this problem may contribute to the difficulty these people have with swing initiation.

Studies have shown that people with PD do demonstrate difficulties in unweighting the stance limb. Patients who are voluntarily unable to start stepping can exhibit near normal stepping when they are rocked from side to side, which causes a shift in weight to occur (Martin, 1967). Examination of the ground-reaction forces during a voluntarily initiated step in PD patients indicated that they do not generate enough force to shift their weight over to the opposite limb. In normal subjects, this movement of the centre of mass (CM) over to the contralateral limb is classified as an anticipatory postural adjustment. It allows the leg to prepare to move into swing. As well, PD patients have difficulty in generating a sufficient vertical ground-reaction force quickly enough to thrust the leg into swing (Burleigh-Jacobs, Horak, Nutt and Obeso, 1997).

The results of these studies indicates that how information concerning loading of the extensor muscles is relayed to the spinal cord and used by the CPG needs to be considered when investigating Parkinsonian locomotion. Group Ib afferents, arising from the Golgi Tendon Organs (GTO's), relay the amount of muscle tension to the spinal cord. The afferents do not make direct connections onto the motorneuronal pools, but connect to them through interneurons. These Ib interneurons also receive information from a variety of different afferent inputs (Ia's, joint, cutaneous) and descending systems (reviewed in Jankowska, 1992). These different inputs can modulate how well the interneurons transmit incoming afferent input onto the motorneuronal pool. There is already evidence that the effects of the group Ib afferents, under static conditions, are modified in PD with regards to the disynaptic connections between group Ib afferents and the motorneurons. Input from these afferents appears to have an opposite effect on synergistic muscles than what is found in normal adults under static conditions (Delwaide, Pepin and Maertens de Noordhout, 1991). Instead of the inhibitory effects of a group Ib conditioning stimulus of the medial gastrocnemius (MG) on the soleus H-reflex seen in normals (Pierrot-Deseilligny, Katz and Morin, 1979; Pierrot-Deseilligny, Bergego and Mazieres, 1983), a trend towards facilitation is produced. This indicates that in PD, one change in the nervous system is how the reflex arc is modulated under a given task.

Evidence to support this concept of a change in the modulation of reflex action in PD has been found in other spinal reflexes. The excitability of the motorneuronal pools seemed to be increased with rigidity in PD (McLeod and Walsh, 1972), probably due to changed input from such descending systems as the reticulospinal tract and others. As well, a study by Martinelli and Montagna (1979) showed that the inhibition seen in the magnitude the soleus H-reflex with non-noxious cutaneous stimulation of the posterior tibial nerve is reduced in PD patients. Tendon jerks are amplified in PD (Hammerstad, Elliot, Mak, Schulzer, Calne and Calne, 1994). The later components (M2 and M3-believed to be transcortical in nature) of stretch reflexes are exaggerated as well with PD rigidity (Tatton and Lee, 1975; Aminoff, Siedenburg and Goodin, 1997). Since spinal reflexes play a role in the generation of the gait pattern, a change in the modulation of reflexes from normal may therefore be one possible component of the gait difficulaties seen in PD patients

If this is the case and if the amount of load placed on the extensor muscles is an important factor in determining when the stance-to-swing transition occurs, it may be that the transmission and utilization of the load information from the extensor muscles is being incorrectly modulated in this disorder. The spinal cord may be interpreting the afferent feedback as if the extensor muscles to be more loaded than they really are, and thus preventing the move into swing from stance. Modulation of the afferent information concerning the amount of load on the extensor muscles has been indirectly examined in Parkinsonian gait (Dietz and Colombo, 1998). The gait patterns of young healthy adults, older age-matched controls and PD patients were studied when unloading the body by a certain percentage of body weight (by 25%, 50% and 75% of body weight). In all three groups, flexor muscle activity was in general little affected by the unloading. However, the activity in the extensor muscles was very load-sensitive as they were activated less with reduced weight. While this effect was seen in all three groups, the degree of sensitivity to the change in load was greatest in the young, normal adults, reduced in the healthy elderly, and the least sensitive in the PD patients. As well, the absolute magnitude of the extensor activity generated during the stance phase was reduced from the young adults to the older, healthy adults to the PD patients. The authors suggested that the decreased sensitivity in the extensor load reflex, first with age and then with the disease, could contribute to the difficulty they have with walking. But they did not produce direct evidence that there was a change in the group I reflex pathway, as they did not test how the reflex pathway might have been modified with the change in load.

Therefore, the purpose of this study was to determine if the effects of the group I afferents during gait were different in PD than those previously found in normal adult walking (Chapter 2 and Chapter 3). Two approaches were taken to examine this issue. The first was to try to replicate the results of the study by Delwaide and his colleagues (1991) under quiescent conditions, where it was found that the inhibitory influence of group

I input on the soleus motorneurons is reduced, and possibly switched to a facilitation. We then extended the testing to walking, to see if the reflex pathway is modulated differently from the quiescent state in PD. It is also important to find out if and how it may be modulated differently than the results found in normal adults during walking, where there is a reduced inhibitory effect, and a possible trend to facilitation. It may be that if the trend is towards facilitation during walking, and the reflex arc is already under a facilitory influence, there is a "summation" of these effects which may result in a greater facilitory effect. This would result in the spinal cord interpreting any amount of load as being greater than what it truly is, and may prevent the stance-to-swing transition. The second approach was to see if a train of electrical stimuli at group I strength to the nerves supplying extensor muscles would cause a change in the durations of the stance phases and step cycles during walking. Electrical stimulus to these afferents has been shown to prolong extension and/or terminate flexion in reduced animal preparations. If activity from descending systems that contribute to the modulation of the activity of the Ib interneurons is absent or reduced in some manner, it may be that similar effects will be seen with these patients as are seen in the animal studies. In addition, in a sub-set of the patients, there was an attempt to examine the muscle activity patterns for locomotion in these patients and how other attentional demands may change the walking pattern. It was noticed during testing of the first few subjects that their gait patterns would change when their attention was distracted away from monitoring their gait pattern. It was postulated that during testing, the subjects were consciously monitoring their walking, and as a result, it was not as "automatic" an activity as seen in normal humans, but required more influence of cortical centres. The distraction condition was added to see if the group I afferent input would modified the patients' stepping when their walking was as "automatic" as it could be.

The results reported here are preliminary, as more subjects with greater locomotor deficits need to be tested. As well, overground walking should be used as it may show a greater effect than treadmill walking does, as the treadmill may be providing cues that the patients use to regulate their step cycles.

5.2 MATERIALS AND METHODS

Two protocols were used in the study. The first protocol examined the effect of a conditioning stimulus of the MG nerve on the magnitude of the soleus H-reflex (Pierrot-Deseilligny et al., 1979, 1983). Previously, this protocol was used to examine differences in the Ib pathway from the MG muscle between the tasks of sitting, standing and walking in young adults (Chapter 2). Here, the same procedures were used. Fewer condition-test intervals were examined to decrease the duration of testing.

The second protocol involved applying a short train of electrical impulses to the tibial nerve at the end of the swing phase to mimic group I input. Stimulation at this point in the step cycle in decerebrate cat preparations caused a resetting of the step cycle by stopping the flexor activity and initiating extension (Guertin, Angel, Perreault and McCrea, 1995). As well, we initially did pilot testing of the stimulation protocol on young normal subjects during the stance and swing phases (not shown). A greater effect on the durations of the phases of the step cycle was seen when the stimulation occurred near the end of swing (a reduction in the duration of the swing phase). Research has indicated that the flexors may be under greater supra-spinal control than the extensors (Capaday, Lavoie, Barbeau, Schnieder and Bonnard, 1999). If this is the case, and the mediating descending influence on the flexor activity is missing or distorted by PD, then stimulating the extensor afferents at this point in time may result in greater inhibition of the flexor half-centre of the CPG. It was hypothesized that stimulating at this point in the step cycle in PD patients would result in the swing phase being terminated and stance initiated.

In three of the subjects, an additional cognitive task was added so that they were distracted. This caused their attention to be diverted away from the walking task. The cognitive task consisted of being asked to answer some simple math and knowledge questions.

Subjects

A total of 11 subjects (age range: 48-80 years), diagnosed with Parkinson's Disease, were studied after obtaining informed, written consent. Most subjects participated in one testing protocol only. Two of the subjects were tested under both protocols on different days. Seven subjects were studied under the first protocol while 5 were studied under the second. One was studied not using either protocol, but his walking was examined to see how a distracting cognitive task would affect his normal gait pattern. Criterion for inclusion in the study was the ability to walk for short intervals (approximately 5 minutes) on a treadmill at a comfortable speed (range: 0.4 to 0.778 m/s). Individuals who suffered from any other neuromuscular disorder that could confound the results were excluded.

Control values for comparison purposes are from the data collected on young subjects as reported in Chapter 2 for normal gait patterns and the conditioned H-reflex paradigm. It should be noted that Delwaide and colleagues (1991) found the same pattern of inhibition in older age-matched control subjects as had been seen in young adults when using this paradigm in sitting.

General Procedures

The subjects did not take their medication associated with PD (in the majority of cases: Sinamet) on the morning of the test session. Most test sessions were held early in the morning to minimize the duration the subjects were off their medications. The test sessions were kept to a length of no more than 3 ½ hours.

A short clinical motor test, taken from Section III: Motor Examination of the Unified Parkinson's Disease Rating Scale (or UPDRS; Fahn, Elton et al., 1987), was conducted at the start of each test session. The clinical motor test was videotaped, such that scoring could be done later by a physical therapist.

For both protocols, Ag/AgCl surface electrodes (1 cm in diameter, placed 1 cm apart) were used to record muscle activity. In procedure #1, both soleus and MG muscle activity was monitored. The soleus electrodes were placed below the insertion of the gastrocnemius muscles. The MG electrodes were placed on the muscle belly where the muscle contracted when stimulated at threshold intensity of the MG nerve stimulation. In procedure #2, soleus and tibialis anterior (TA) muscle activity was recorded. Vastus Lateralis (VL) and Biceps Femoris (BF) were also recorded in one subject. The signals were amplified and high-passed filtered at 10 Hz. Three force-sensitive resistors (FSR's) were placed under the heel and heads of the first and fifth metatarsal of the left foot. The FSR's were sandwiched between a metal plate and a custom-cut insole and placed in the subject's shoe (modified from Zehr, Stein, Komiyama and Kenwall, 1995). These transducers indicated when the foot was in contact with the ground. All signals were recorded on VHS videotape using an A/D VCR adapter (A.R. Vetter Co. Inc., Rebersburg, PA, USA).

Procedure 1: Condition-Test Stimulation of Soleus H-Reflex:

A complete description of this protocol can be found in a previous paper (Chapter 2). Seven subjects were examined using this procedure. In brief, a stimulating electrode was placed in the popliteal fossa at the best location to generate an H-reflex in the soleus muscle. A second stimulating electrode was situated (approximately 5 cm medially and distally to the first electrode) over the MG nerve. The anodes for each of the stimulating cathodes were placed on the anterior-lateral side of the thigh, just above the patella, for the tibial nerve stimulation and on the anterior-lateral side of the shin, just distal to the tibial plateau for the MG nerve stimulation. The electrode over the MG nerve applied a conditioning stimulus at short time periods (condition-test intervals) prior to stimulation of the tibial nerve. To reduce the time involved in the data collection, a small set of condition-test intervals (5, 6 and 7 ms) was examined. These condition-test intervals were chosen as they showed the greatest inhibition of the soleus H-reflex during sitting in our previous study (Chapter 2). These same intervals showed the greatest facilitation of the soleus H-reflex in Parkinsonian subjects (Delwaide et al., 1991).

With the subject sitting, an electrical pulse (duration: 1 ms) was delivered to the tibial nerve at the politeal fossa to generate an H-reflex in the soleus. The stimulus intensity used was one that elicited an H-reflex that had a peak-to-peak amplitude that was 10-15% of the maximum M-wave. This was the control H-reflex. Alternating with the control H-reflex, a conditioning electrical stimulus (single pulse of 1 ms duration) was delivered to the

MG nerve just prior to the tibial nerve stimulation (at different condition-test intervals). The stimulus to the MG nerve was set at the intensity just below motor threshold for the MG muscle to selectively recruit the group I afferents. Stimuli were delivered at 3-second intervals. Groups of 50 stimuli were recorded, so that 25 control reflexes and 25 conditioned reflexes were collected. If the variability of the control H-reflexes generated exceeded 20% of the average mean H-reflex, the trial was either excluded, or analyzed more extensively off-line.

During walking, the stimuli were presented during mid-stance of every other step. The stimuli were presented at a fixed delay from the start of the stance phase (400 to 500 ms after heel contact). The control and conditioned reflexes were again elicited alternately (40-50 each).

The data were analyzed online, using a custom-designed computer program that calculated peak-to-peak measures of the control and conditioned soleus H-reflexes. The data were band-passed filtered from 10 to 1000 Hz and A/D converted (at 2850 Hz) before averaging. As well, the data were analyzed off-line being A/D digitized (Axotape/Axoscope, Axon Instr. Inc., Foster City, CA) at 2500 Hz such that individual peak-to-peak values for each H-reflex generated during the trials could be recorded. In subjects where the variability of the control reflex was too great (exceeding the 20% variability criterion), the individual control data points that exceeded the average mean +/- 2 standard deviations on each side of the mean were deleted, as well as the following conditioned reflex (regardless of size).

Procedure 2: Effect of Stimulus Trains:

The subjects walked on the treadmill at their comfortable speed for approximately 5 minutes. Short (100-200 ms) or long (300-400 ms) trains of stimuli (1 ms pulses at 100 Hz frequency) were applied to the tibial nerve at the popiteal fossa, at stimulus intensities just below that of motor threshold for the soleus muscle. This was accomplished by stimulating the tibial nerve and examining when an H-reflex and an M-wave were generated within the soleus muscle during walking. Then, the stimulation intensity was set at a level just below the stimulus intensity of the threshold for the M-wave. This was verified by the absence of an M-wave in the muscle with the stimulation. This intensity still generates an H-reflex, indicating that the group I fibers are being recruited. It has been known for several decades that a percentage of both group Ia and Ib afferents are activated at electrical stimulus intensity levels that are below the intensity needed to generate a M-wave. The trains were applied during randomly selected steps throughout the walking trial. The stimulus trains were triggered after a fixed delay from the beginning of heel contact, such that the train began just prior to the next heel contact. Twenty to thirty trains of a given time duration were presented during each walking trial.

The data were analyzed off-line, to determine the durations of the step cycle, stance phase and swing phase for steps with and without stimulation. Off-line analysis included the EMG being full-wave rectified and low-passed filtered at 30 Hz. It was then A/D converted with the FSR data at 350 Hz (Axotape/Axoscope, Axon Instr. Inc., Foster City, CA). Using a custom built computer program, average durations of the step cycles, stance and swing phases were calculated for: steps where no stimulation occurred (normal or prestimulation); steps where the stimulation was applied (stimulated); and the steps immediately following the application of the stimulus trains (post-stimulation).

Cognitive Task:

Three subjects studied were asked, while walking on the treadmill at their comfortable speed, a number of simple math (eg. 70/10 = X) and declarative memory questions (eg. Name any animals you can think of whose name begins with the letter "D"). These questions placed a cognitive demand on the subject that diverted their attention away from the walking task. The subjects were asked the question by an experimenter situated just forward and to the side of them. If they could not answer the question within a reasonable time frame (generally 5 seconds for a math question and 10-20 seconds for a declarative memory question), the experimenter would move on to the next question

Statistical Analysis:

For procedure #1, repeated measures ANOVA's (2 X 3 design) were used to determine whether the conditioned H-reflexes differed in peak-to-peak magnitude from the control H-reflexes for each C-T interval for both sitting and walking. The conditioned H-reflex/control H-reflex ratio for each C-T interval was compared between sitting and walking using a repeated measures ANOVA. Significance level was set at $p=0.05$. ANOVA's were also used to analyze differerences between the results obtained from the PD patients and those from young, non-neurologically impaired subjects (results of Chapter

2).

For procedure #2, a one-way ANOVA was used to determine if there were any significant differences in the durations of the step cycles, stance phases or swing phases of the normal, stimulated or post-stimulation steps. Significance level was also set at p=0.05.

Clinical Analysis:

Clinical measures were scored using the UPDRS guidelines (Fahn, Elton and members of the UPDRS Development Committee, 1987; Teaching Tape: Goetz, Stebbins, Chmura, Fahn, Klawans, and Marsden, 1995). The scoring was done by a physical therapist, who viewed the videotape of the clinical motor test after the actual testing session, and who was experienced with the UPDRS scoring system. It should be noted that the physical therapist also was familiar with the subjects as she recruited them from the clinic where she works. The scores were tabulated by calculating the average rating given for each task in the clinical motor test across subjects, as well as indicating the number of subjects at each rating level. The UPDRS operates on a 5-point rating scale, where 0 indicates normal function and 4 indicates the most severe impairment. For most of the tests, a score of 2 would indicate mild to moderate impairment. As well, the physical therapist evaluating the patients also provided a score for each patient on the 5-stage Hoehn and Yahr clinical rating scale (Hoehn and Yahr, 1967). The Hoehn and Yahr scale is a 5-point scale (Stage I-V). Stage I is classified as "unilateral involvement only, usually with minimal or no functional impairment". Stage II is "bilateral or midline involvement, without impairment of balance". Stage III has "first sign of impaired righting reflexes... Functionally the patient is somewhat restricted to his activities... Patients are physically capable of leading independent lives, and their disability is mild to moderate." Stage IV is "fully developed, severely disabling disease, the patient is still able to walk and stand unassisted but is markedly incapacitated, and Stage V is classified as "Confinement to bed or wheelchair unless aided" (Hoehn and Yahr, 1967, p.433).

5.3 RESULTS:

Clinical Tests:

All portions of the UPDRS clinical tests were scored, except for the measurements of rigidity and the postural instability measure. These were not scored, since they depended on tester-subject interaction, which could not be quantified. The averaged scores across subjects of the other motor tests are shown in Figure #5.1. The average scores indicated that the patients were at most moderately affected in terms of overall motor function. Most of the scores fell in the 0-2 range for each of the clinical tests. For the majority of the motor tasks, the average score fell between a rating of 1, which refers to a slight impairment, to that of 2, which indicates mild to moderate impairment. The only averaged scores that fell above 2 were for right-and left-hand finger taps and the amount of mobility of the face.

Individual clinical test scores show that there was more difficulty in accomplishing the upper limb movements than in the lower limb for most subjects. A greater portion of individual scores fell at or above UPDRS scores of 2 (mild to moderate) for such tasks as tremor or finger taps than those for the tests that involved the lower limbs (arising from a chair, standing posture, gait, and bradykinesia). For example, the range of scores for the left hand forming a fist (hand clenching) was 0 to 3, with one subject scoring 0, 4 subjects scoring 1, 4 subjects scoring 2 and 2 subjects scoring 3. On the other hand, the scores for the gait motor test was 1 subject scoring 0, 9 subjects scoring 1 and 1 subject scoring 2.5.

On the Hoehn and Yahr scale, 1 patient was rated midway between Stages I and II, 4 patients were at Stage II, 3 patients were between Stages II and III and 3 patients were at

Stage III.

EMG profile of Parkinsonian gait resembles that of normal walking.

Figure #5.2 shows two typical examples of the parkinsonian EMG profiles during treadmill walking, as well as one young adult unimpaired subject. The patients in general tended to walk at a slower speed (0.44 to 0.7 m/s) than young normal adults, who walked comfortably at 0.9 to 1 m/s (see Chapter 3). The patterning of their EMG activation was in general similar to normal walking in terms of when the muscles were activated.

The patterns were not exactly the same. In figure #5.2, the durations of the step cycles of a young normal subject and the patients have been normalized to 100% for comparison purposes. While the general patterns of activity are the same (soleus activated during stance, TA activated during swing and swing-to-stance transition) there can be individual variations. There is greater activation of the quadriceps in the parkinsonian subject DB than seen in the normal subject. This is probably due to the fact that Subject DB walked fairly flat-footed (as seen from the FSR data, where the heel does not have the abrupt rise associated with a strong heel contact). There was also some flexion in the knee that did not go into full extension during stance. The activity in the quadriceps was probably to keep the limb from collapsing. The second burst in TA, used to stabilize lowering of the toe after heel strike, is reduced, though still present, in subject DB. Subject ST showed a prolonged activation of the heel FSR, indicating that the heel remained on the ground, bearing a large amount of load, until late in the stance period. This is reflected in the activity of his Soleus EMG, which remained relatively quiet until just before push-off.

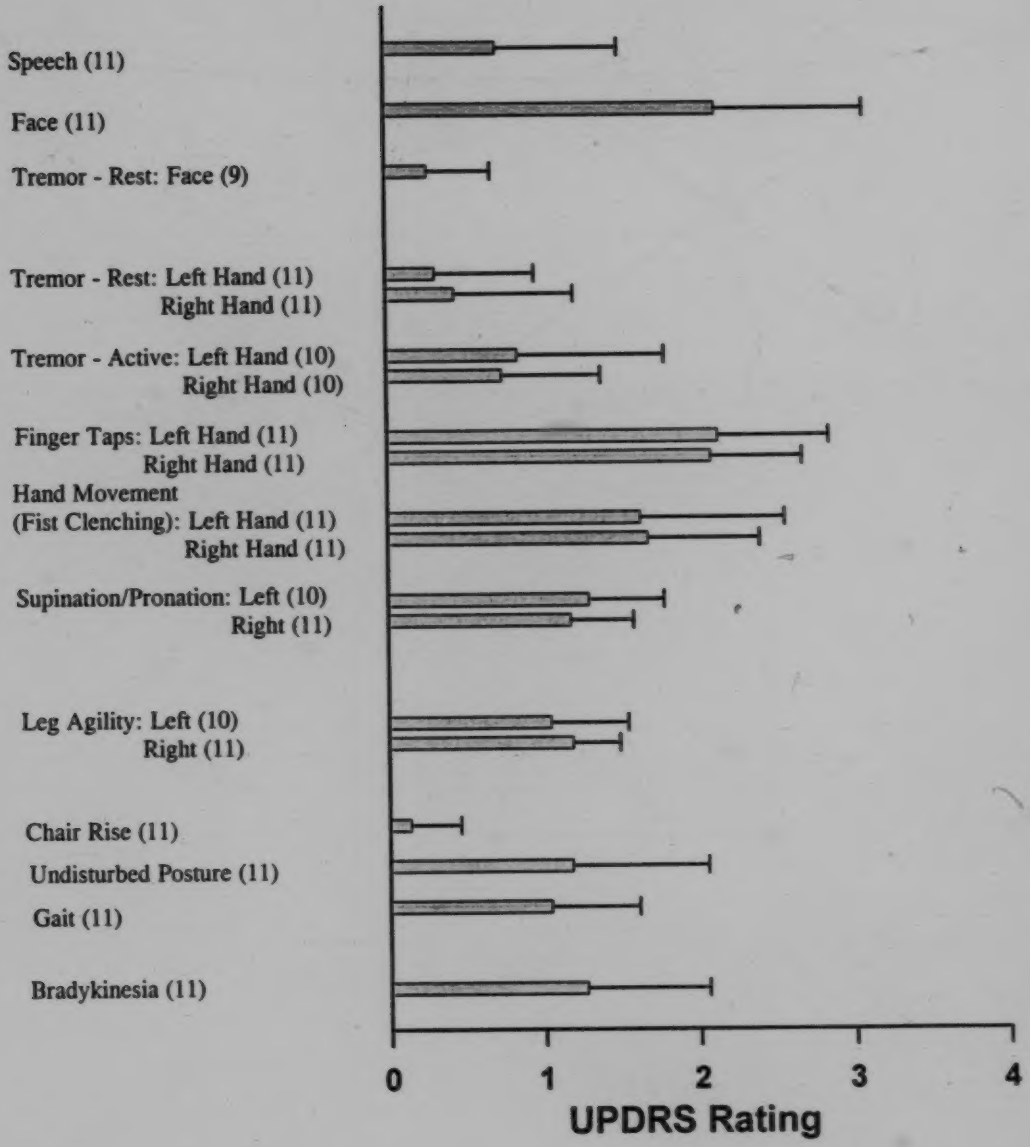

Figure 5.1: Average values across subjects for each of the UPDRS motor clinical tests. The UPDRS rating scale goes from 0 (no impairment) to 4 (extreme disability) for each of the tests studied. As can be seen, the highest average values can be seen in the face and active hand movements, while lower averages are found in the passive hand activities and tasks involving the lower limbs. Error bars indicate standard deviations.

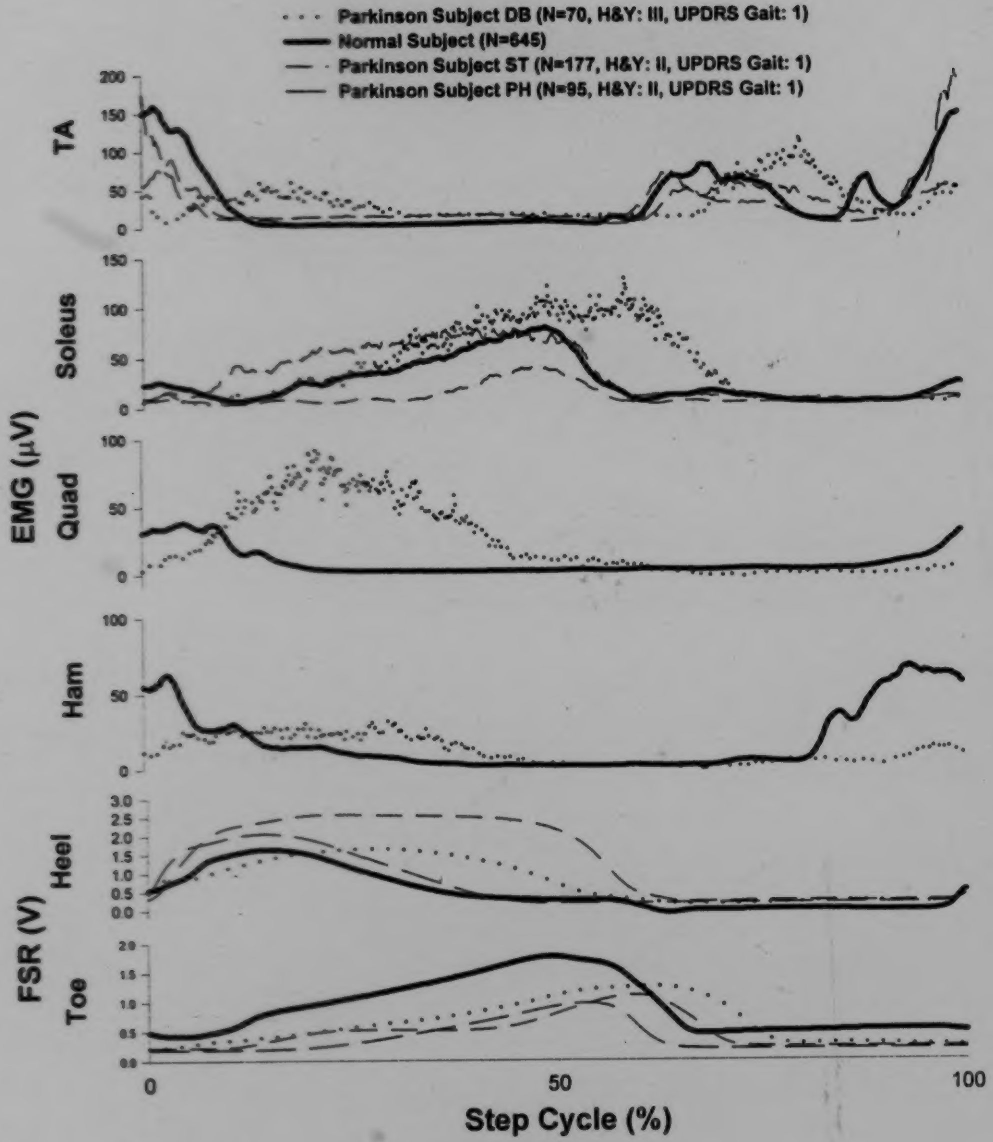

Figure 5.2: Examples of individual parkinsonian EMG and force profiles during walking compared to a neurologically normal young adult. Step cycle times have been normalized to 100 percent to show differences in profiles for the same percentage of the step cycle (0% is heel contact). The **N** in brackets in the legend refers to the number of steps that went into calculating the average profiles. **H&Y** refers to the subject's rating on the Hoehn and Yahr scale. **UPDRS Gait** refers to the subject's score on the gait portion of the UPDRS scale. Quadriceps and hamstring data were only recorded on Parkinson subject DB.

Lack of Inhibition of Soleus H-Reflex in Parkinson's patients during sitting:

The ratios of the conditioned H-reflex compared to the control H-reflex from two subjects are shown in Figure #5.3. While the subject depicted in A/ showed the trend towards a facilitation of the peak-to-peak H-reflex magnitude with the conditioning stimulus that Delwaide and his colleagues found during sitting, the subject shown in B/ did not. When the results of all 6 subjects are pooled, no significant difference was seen between the magnitudes of the conditioned and control H-reflexes at any of the 3 condition-test intervals that were studied (5-7 ms) during sitting (Figure #5.4). Instead, a trend towards facilitation was seen at the 5 ms C-T interval, though it was not significant. This may be due to the fact that the results in sitting were quite variable across patients in terms of the degree of inhibition/facilitation the conditioning stimulus generated on the magnitude of the soleus H-reflex across the different C-T intervals.

Analysis of Variance statistics were run to see if the PD patients results were significantly different than those seen in young non-neurologically impaired adults (Chapter 2). During sitting, across the 5-7 ms C-T intervals, the PD patients' results were highly significantly different than those of the young adults across all three C-T periods examined (p=0.0000204). The direction of results indicated that the magnitudes of the PD patients' H-reflexes with conditioning compared to without were less inhibited than that of normals. Therefore, the inhibition of the soleus H-reflex with the conditioning MG nerve stimulation seen in the majority young non-neurologically impaired adults (Pierrot-Deseilligny et al, 1979, 1983; Study 1: Chapter 2) is not found in these patients, indicating that there is a change in the modulation of this reflex arc with PD patients.

Effect of Condition Stimulus on Soleus H-Reflex during Walking:

During walking, no clear effect was seen on the conditioned soleus H-reflex as compared to the control, when pooled across subjects (Figure #5.5), as there were no main effects found in the ANOVA comparing the two conditions. The average pooled data show no discernable trend in terms of the data being inhibited or facilitated by the conditioning stimulus, as the 5 and 6 ms C-T intervals showed 7.6% and 4.9% inhibition respectively, while the 7 ms C-T interval showed 6.0% facilitation. There was a significant interaction effect (p=0.0322) between the two factors studied (factors: C-T interval and control/condition). Again, a great variation was seen individually across the different C-T intervals.

In comparing the results during walking for the PD patients to those of young, non-neurologically impaired adults, there were no significant main effects of the conditioned/control H-reflex ratios at the different C-T intervals between the two groups. There was a significant interaction of the results when considering both the C-T interval and if the subject was a PD patient or non-neurologically compared (p=0.00397). Student's T-tests comparing the PD group with the normal group showed that there was a significant difference between the results of each group at the 5 ms C-T interval (p=0.00572), where the PD subjects' results showed a greater amount of inhibition with the conditioning stimulus during walking. However, at the 6 and 7 ms C-T intervals, the results from the two groups were not significantly different (6 ms: p= 0.059975; 7 ms: p= 0.067275).

Comparison of H-Reflex Condition/Control Ratios between Sitting and Walking:

Five of the seven subjects had data collected during both sitting and treadmill walking. Two subjects did not have reliable data in both tasks as one subject's walking trials had been collected during overground walking, which had a number of complications with respect to timing of the stimulus and was not included. An H-reflex could not be generated during sitting in the other subject, though one was found during walking. For the 5 subjects that could be included in the comparison between sitting and walking, the comparison of the condition/control ratios for the peak-to-peak H-reflex magnitudes showed no significant difference between sitting and walking at any of the C-T intervals ($p = 0.124$, Figure #5.6)

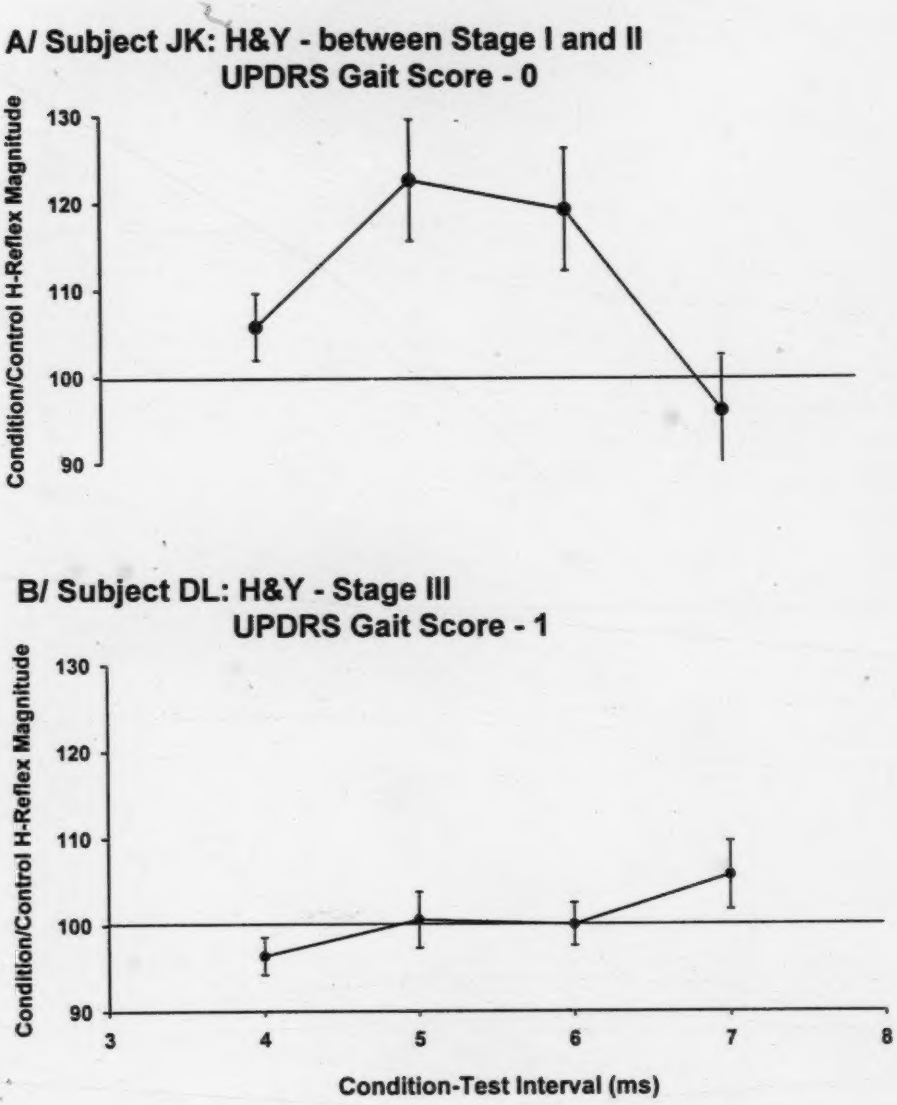

Figure 5.3: The results of 2 parkinsonian subjects during the static condition of the control-conditioned H-reflex paradigm. While in A/ subject JK showed the facilitation of the H-reflex with conditioning stimulus at disynaptic latencies reported by Delwaide and colleagues (1991), B/ subject DL did not show the facilitation, but instead, the conditioning stimulus had almost no effect on the magnitude of the H-reflex. Error bars represent the standard error.

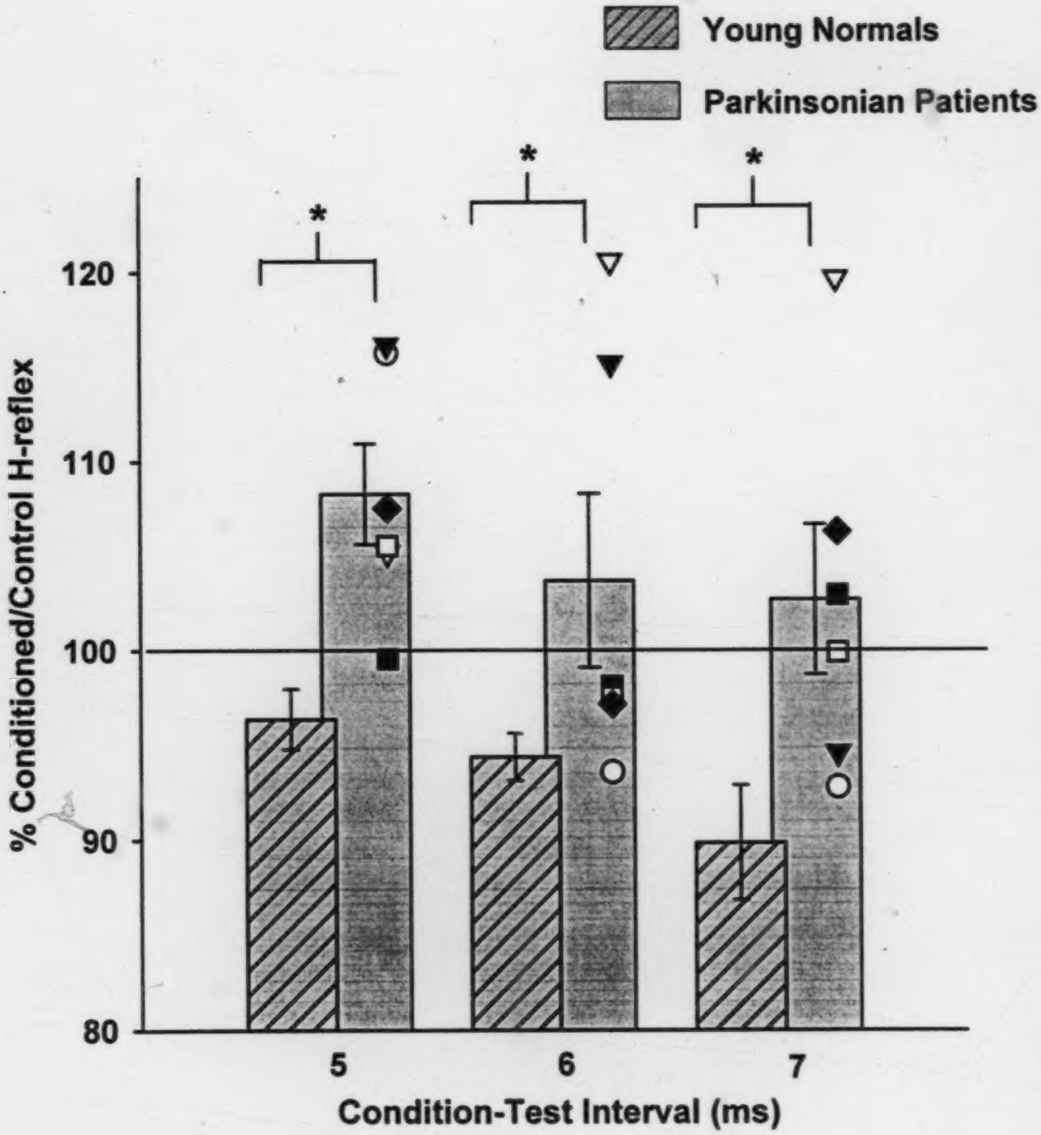

Figure 5.4: Individual scores (symbols) and averaged across-subject data (solid bars) of the conditioned compared to control value ratios for H-reflex magnitude for the parkinsonian subjects for 3 condition-test intervals (5-7 ms) in quiet sitting. The crosshatched bars present averaged control subject values (N= 10, see Chapter 2). The error bars represent the standard error. "*" indicates significant differences between the patients and non-neurologically impaired subjects at the $p<0.05$ level.

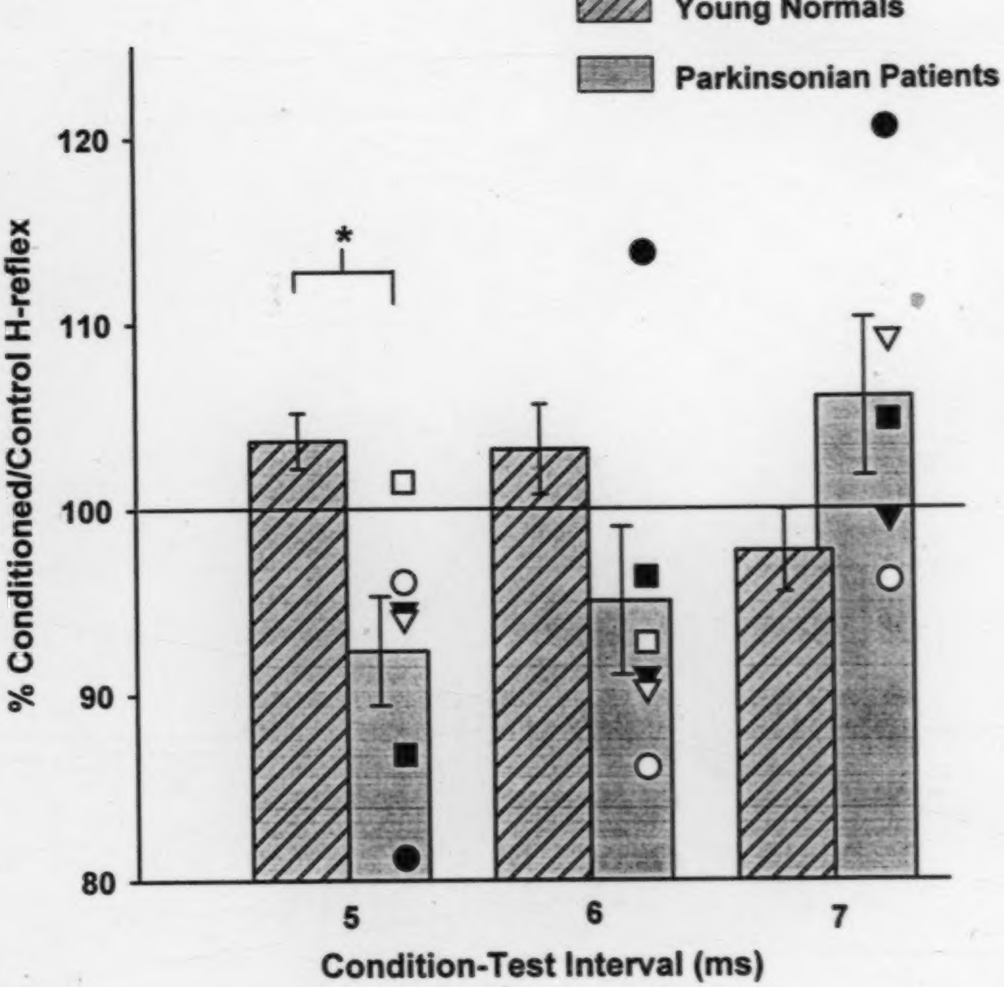

Figure 5.5: Individual scores (symbols) and averaged across-subject data (solid bars) of the conditioned compared to control value ratios for H-reflex magnitude for the parkinsonian subjects for 3 condition-test intervals (5-7 ms) during walking. The crosshatched bars present averaged control subject values (see Chapter 2). The error bars represent the standard error. "*" indicates significant differences between the patients and non-neurologically impaired subjects at the $p<0.05$ level.

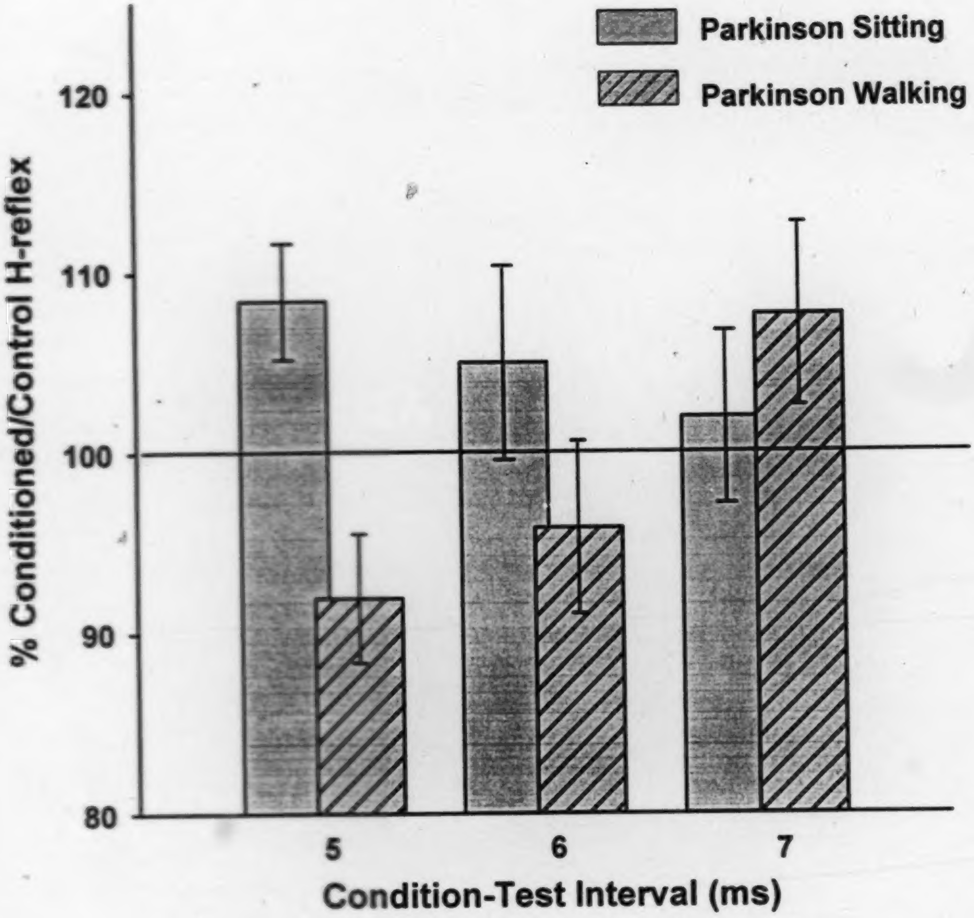

Figure 5.6: Comparison of the average condition-test H-reflex magnitude ratios for the 5 subjects where data was collected in both sitting and walking. The error bars represent the standard error.

Effects of Stimulus Trains on the Different Phases of the Step Cycle:

In this protocol, a train of stimuli of an intensity that was at or just below the motor threshold for soleus activation was applied to the Tibial nerve during the swing phase of walking. Five subjects were studied, but one could not tolerate the levels of stimulation that would activate the motorneuron axons (motor threshold) and thus generate an M-wave when the stimuli were presented as a train. Therefore, only 4 sets of data are included in these results. In the patients, the stimulation of the group I afferents caused a statistically significant change in the duration of the step cycle, as the step where the stimulation continued into the stance phase is shorter (p=0.019) than the step where stimulation started in the swing phase. However, this difference amounts to 20 ms, or 1.5% of the normal step cycle duration, so the functional effect is rather modest. As well, this slight difference does not appear to be due to a consistent change in either of the stance or swing phases, as there was no significant differences in the durations of these phases of the step cycle across the normal or stimulated steps (see Figure #5.7). The overall step cycle duration only changed on average 20 ms between the three different step conditions, while the swing time varied by only 11.8 ms and the stance time varied by 15.5 ms.

Effects of Attentional Demand on the Gait Pattern:

In all of the three subjects studied, additional cognitive demands affected the walking patterns. Figure #5.8 shows the effects on the walking pattern for the most affected subject. The effects on the subjects were that distraction caused a significant shortening of the overall step cycle and the durations of the individual phases. In Subject 1, the step cycle duration decreased 8.56% (1413 ms to 1292 ms) and the stance phase duration decrease by 8.14% (921 ms to 846 ms). For Subject 2, the step cycle duration decreased 10.7% (1140 ms to 1018 ms), while the stance phase decreased by 8.27% (762 ms to 699 ms). Subject 3 (shown) had the step cycle decreased by 30.89% (2444 ms to 1689 ms) with distraction. The stance phase went down 17.79% (1764 ms to 1452 ms). As well, in Subject 1 and Subject 3 (shown in Figure #5.8), the burst in TA that controls the descent of the foot after heel contact is missing while distracted, though it is present when the subjects were thinking about their walking. In Subject 2, the TA burst was still present, and slightly enhanced in amplitude. From the FSR data, with distraction, the force generated on the heel with foot contact with the floor is less, though the force placed on the toe is approximately the same during push-off. Both of these effects contribute to the shuffling pattern that developed in the gait of the subjects while they were being distracted from consciously monitoring their walking. The fact that the walking pattern did change with distraction indicates that even while walking on a level treadmill at a steady speed, the walking is not strictly automatic in nature.

Parkinson Train Data (300 ms, 100 Hz, mid-swing)

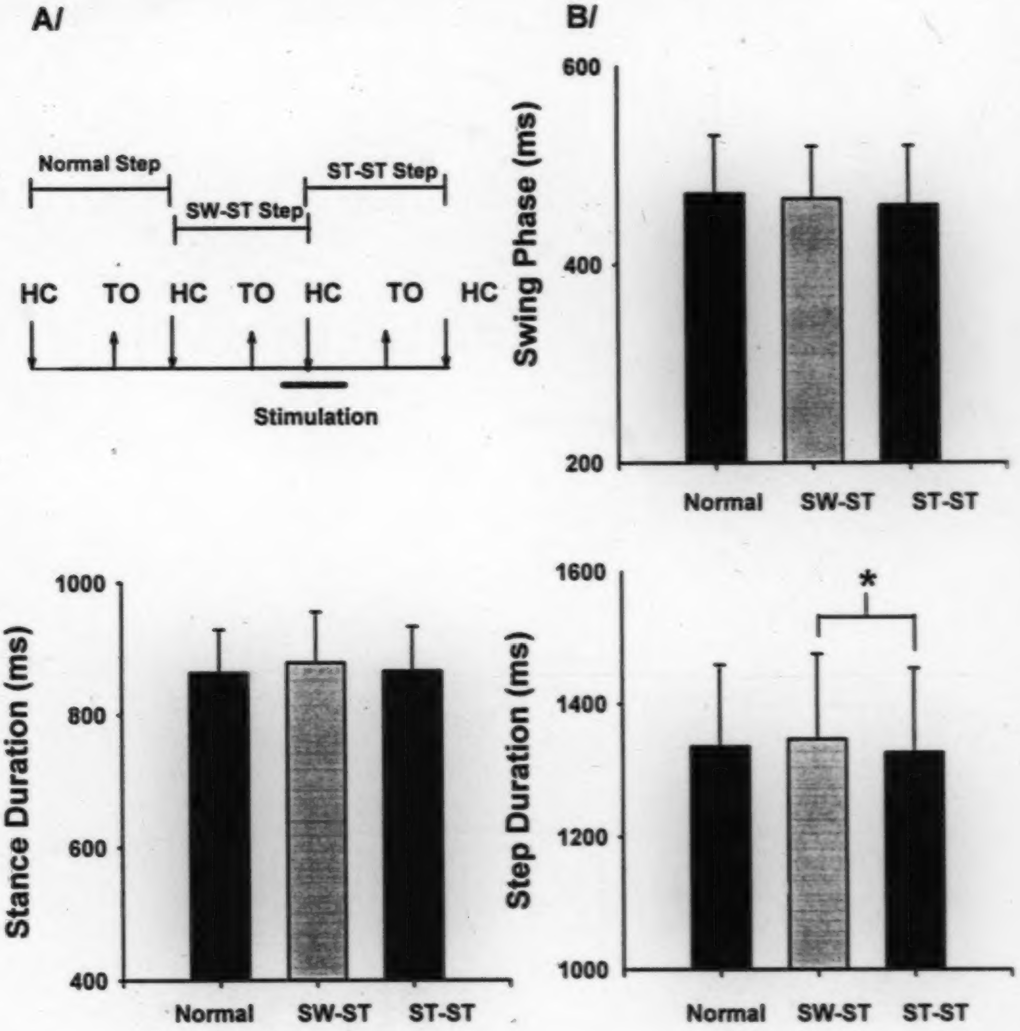

Figure 5.7: Results of the stimulation train of the tibial nerve. A/ Cartoon of the steps compared in the analysis. B/ Comparison of the durations of the step cycle, swing phase and stance phase of the steps: prior to the stimulation train to the tibial nerve at the end of swing *(normal.)*; with the beginning of the stimulation train at the end of the swing phase*(SW-ST.)*; the end of the stimulation train at the beginning of the stance phase *(ST-ST)* in the step following the SW-ST step. The error bars represent standard error. "*" indicates significance at the $p<0.05$ level.

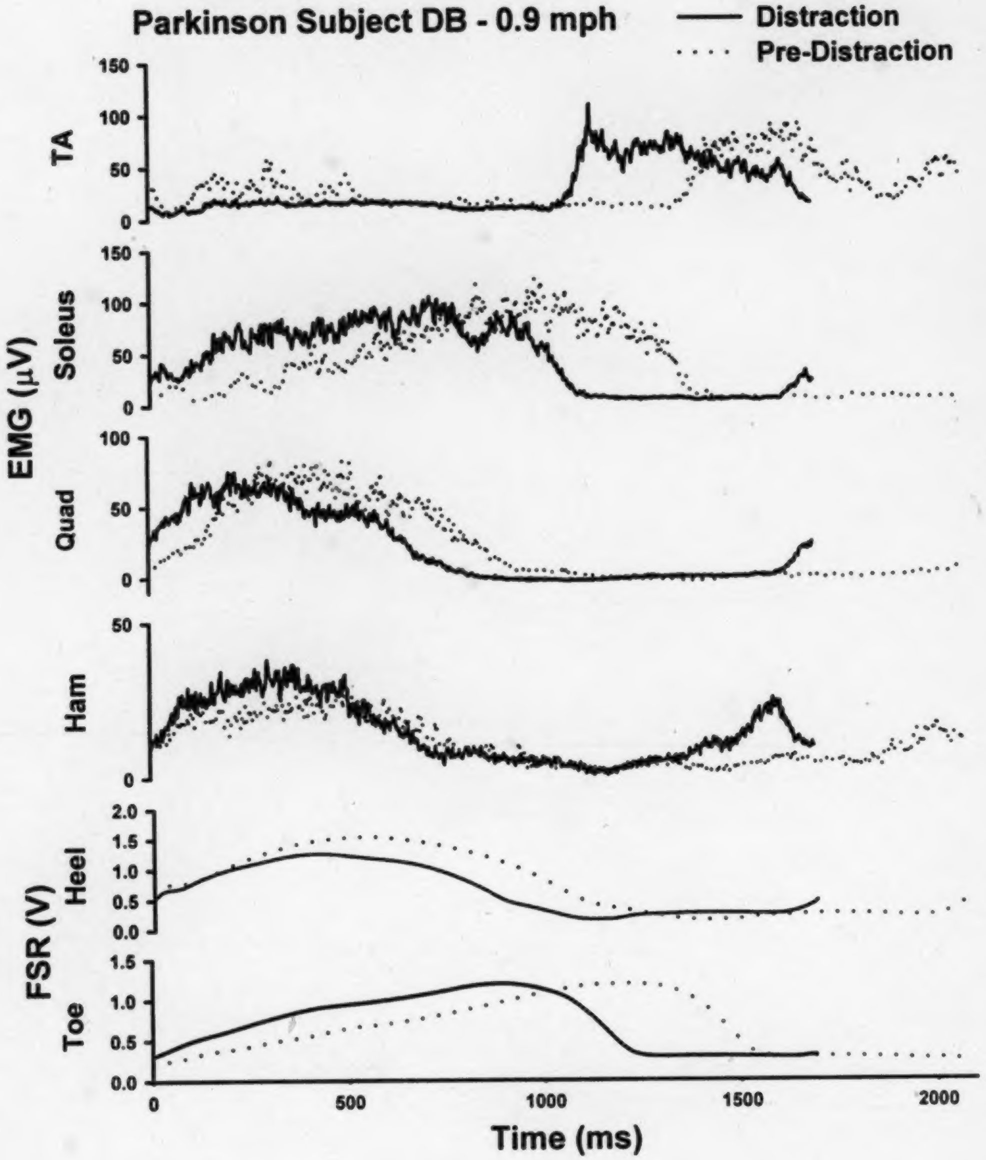

Figure 5.8: Effect of a distracting cognitive task on the EMG and force profiles of Parkinsonian subject DB. Note that the distraction led to a shorter step cycle duration, as well as a loss of the second burst (stance-to-swing transition burst) of TA. As well, the force profile collected from the FSR mounted on the heel tends to indicate that there is less force placed on the heel with distraction at the start of stance.

5.4 DISCUSSION:

The primary finding of these experiments is that stimulation of the group I afferents in extensor muscles in PD patients appears to have very minor effects on conditioning the magnitude of the soleus H-reflex in sitting or walking, and on durations of the different portions of the step cycle. An interesting additional result was the apparent change in the gait pattern when the subjects were distracted from concentrating on their walking by adding a cognitive task. This might indicate that the walking task in parkinsonian patients is not as "automatic" as that seen in normal human walking, and that they may require to access different control systems than normal to generate a productive gait pattern. Speculations as to why this development may occur are discussed at the end of this section.

Parkinsonian Gait:

All our subjects were able to walk independently on a treadmill for at least 5 minutes at a stretch. In terms of their clinical test scores, on the UPDRS clinical motor gait sub-task, 9 of the 11 subjects scored a rating of 1 (one subject scored a rating of 0 or "normal", while the other scored between a 2 and a 3, considered a "severe disturbance of gait"). As such, in terms of their gait, the majority of our subjects' gaits would be described as "walks slowly; may shuffle with short steps, but not festination or propulsion" (Fahn et al., 1987). However, even though their scores were relatively low, it should be noted that this is while they were concentrating on their walking (see later in Discussion for effects of attentional demand on motor tasks in PD). Still, even with the relatively mild impairment to walking, there were some differences seen in the activation patterns of the lower limb muscles and the forces produced as a result. They tend to walk flat-footed, with a change in the ground-reaction force profiles, and in some subjects, different muscles have slightly different activation patterns, especially if the PD subject's attention is directed away from their walking. However, these people should still be considered as having relatively mild gait disorders, as even off their medication they could still perform the walking task on the treadmill for several minutes. For future studies, it would be beneficial to examine patients with more severe gait impediments so that any changes in reflex modulation from the normal are possibly more clearly magnified or reduced.

The Effect of a conditioning MG stimulus on the Soleus H-reflex is different between Normal and Parkinsonian Subjects in sitting:

It had been shown that, during sitting, a conditioning stimulus of the MG nerve, at condition-test intervals indicative of a disynaptic reflex pathway caused an inhibition in the magnitude of the H-reflex generated in normal adults (Pierrot-Deseilligny et al, 1979, 1983; Stephens and Yang, 1996). Delwaide et al. (1991) showed that in PD patients, there is less inhibition or a switch to a facilitation of up to 7.5% at these same latencies. The results of this study agree with the prior results that there is a reduction in the amount of inhibition seen during sitting in the PD patients. In fact, there appears to be no statistically consistent difference between the magnitudes of the soleus H-reflexes generated in either the control or the conditioned stimuli. It should be noted however that the PD patients were studied with a single conditioning stimulus to the MG nerve. This was due to the time constraints in testing these subjects. This was a slightly different protocol than was used with the young control subjects (Chapter 2) where the conditioning stimulus might consist of 2-4 pulses to the MG nerve, which were needed to produce a significant inhibition of the soleus H-reflex magnitude. However, other studies have used only a single pulse (Pierrot-Deseilligny et al., 1979, 1983; Delwaide et al. 1991). These results are consistent with the results of those studies.

The present results of the PD subjects indicate a clear trend away from the inhibition found in the normal young adults. This trend is towards facilitation, as reported by Delwaide's group. However, not all the PD subjects showed an excitatory influence on the soleus H-reflex with the MG stimulation (See Figure 5.3). It may be that the subjects we studied did not have enough of impairment in their lower limbs to result in a clear facilitation of the soleus H-reflex with the conditioning stimulation of the MG nerve. Still, the comparison of the results from the PD patients to the young adults shows that there is a difference in how this reflex is modified with group I afferent input. The mechanics of how that modulation is changed and why the difference in modulation occurs cannot be discerned from this study. It is interesting to note that the Parkinsonian patients share this change in the modulation of the H-reflex with group I conditioning stimulation with patients that suffer from hemiplegia spasticity (Delwaide and Oliver, 1988). However, people with complete and incomplete spinal cord lesions show the same type of modulation as seen in normals (Downs, Ashby, and Bugaresti, 1995). This may be another indication that it is defective descending input that results in this modulation, as opposed to an absence of descending input.

MG Condition Stimulation on the Soleus H-Reflex during Walking has an inconsistent effect in Parkinsonian subjects:

The results of the present study show that there is not a clear inhibition or facilitation at disynaptic latencies for the MG conditioning stimulus on the soleus H-reflex during walking. This is consistent with the effects seen in the normal subjects in our previous study (Chapter 2), where there was no significant effect seen between the conditioned and control data for the same C-T intervals as used in this study. The effect of the conditioning stimulus during walking on the group I reflex pathway, as monitored with the soleus H-reflex, showed an inhibitory influence at the 5 and 6 ms C-T intervals, but a facilitatory influence at the 7 ms.. However, none of these were statistically significantly different from the control reflex magnitude. There was one significant difference found between the PD patients and the young normal adults in that at the 5 ms C-T interval, the patients' results indicated there was more inhibition of the magnitude of the H-reflex with conditioning stimulus than seen in the results of the young adults. We had hypothesized that there might be a greater facilitation of the Group Ib reflex arc. This was not found. If anything, the reverse seemed to be true. From these results, it is difficult to interpret how the Group I reflex arc is modified in PD patients and if any differences could be seen between this population group and normals during the walking task.

There is no clear facilitation or inhibition during walking in either the control subjects or the PD patients. This may indicate that during the task of walking, at least while walking on the treadmill in a controlled environment, with relatively little change in postural stability, the afferent information from the medial gastrocnemius is being processed at the spinal level, but does not have a huge effect on the activation of the soleus motorneuronal pool. Thus, changes in this input may have little effect on the gait cycle.

Stimulation of Group I afferents has no significant effect on the timing of the step cycle:

The stimulation train had no significant effects on the durations of the stance or swing phases of the PD patients when walking. A slight significant difference showed up statistically in the durations of the step cycles between the steps where the stimulus was started in late swing, which was longer than the subsequent steps where the stimulus continued into the stance phase. However, the difference in duration (1.5% of the normal step cycle duration) is modest and may not have much functional significance. It had been hypothesized that stimulation at group I strength intensities at the end of swing would bring the leg down into stance sooner, as the afferents would indicate increase in load. The resulting step cycle and swing phase of the stimulated step would be shorter and the stance phase of the next step would be prolonged. This did not occur. There was no functionally significant effect on any phases of the step cycle, and the one statistically significant difference seen in the duration of the step cycle was in the opposite direction than what was expected. However, it should be noted that for most of the subjects studied, the subject was able to concentrate solely on their walking while on the treadmill. No other attentional requirements were placed on them. There have been some studies that show that when competing attentional demands are placed on PD patients, various tasks become impaired (Morris et al. 1996). They found that when PD patients were trained on a walkway with either visual cues or concentrated on maintaining a mental picture as to how long an appropriate normal stride length is, they could maintain this normal gait for at least 2 hours. However, when they were given competing attentional tasks or when they were not concentrating on their walking, they reverted back to their own gait pattern. The authors felt this suggested that PD patients are capable of generating a normal gait pattern but that they need either visual cues or attentional strategies to do so.

Effects of Attention on Parkinsonian Gait:

In three subjects, we placed additional attentional demands on them while they walked. This was done by asking them various types of questions (such as simple mathematical (ie. 50/10 = X) and basic knowledge questions (ie. Name 5 Canadian provinces). In the three subjects studied, the distraction caused a shortening of their step cycles. Two subjects' EMG profile showed that with distraction, the second burst of the TA, which is used to lower the foot after heel strike, was lost when they didn't concentrate on their walking (See Figure #5.7). It should be noted that on the Hoehn and Yahr scale that one subject was placed at Stage III, though the UPDRS scores from the clinical motor test for his lower limb tended to indicate mild impairment. Another subject's Hoehn and Yahr rating was between the second and three stages, though again the impairment in his lower limbs for the tasks on the clinical portion of the UPDRS was found to be rather mild. It appears from the few subjects reported here that when their attention was directly away from their walking, they reverted to a gait pattern much like that reported by Forssberg and his colleagues (1984), where the foot tends to land more flat footed and the steps are smaller. More work needs to be done on this area of the role of attention during walking and how attentional demands might affect changes in the utilization of afferent feedback. It could be that during the task when the PD patients are concentrating on their walking, as seen on the treadmill, their conscious and subconscious supraspinal input is reducing the role afferent feedback could have. Especially interesting to note is the change in the activation of TA with and without distraction. Loss of the second burst, which controls the descent of the forefoot after heel strike, could possibly indicate that this activation of the muscle is to a greater degree under supraspinal control than that of other muscles' activation, which did not change substantially with the loss of attention. There is evidence that the supraspinal centres may be more linked with the segmental motor circuits involved in the control of the flexors during both the stance and swing phases of walking (Capaday, Lavoie, Barbeau, Schnieder and Bonnard, 1999). Transcranial magnetic stimulation of the motor cortex at various times during the step cycle evokes motor responses in the flexor TA during the swing phase that is facilitated in size from those evoked during static contraction of the muscle at matched EMG levels (Schubert, Curt, Jensen and Dietz, 1997). The effect of the transcranial magnetic stimulation was not as profound on the extensor gastrocnemius. Thus it appears that the supraspinal centers may have greater control over activity in the flexor muscles than they do in the extensors.

Ways that Impaired Basal Ganglia function can influence Walking:

There are at least two pathways from the supra-spinal centres that could to be impaired in PD. The first is through the peduncIo-pontine nucleus (PPN), which in lower mammals has been shown to receive afferents from the entopeduncular nucleus (EN - the animal equivalent to the globus pallidus) and substantia nigra, and project efferents to the mescencephalic locomotor region (MLR) (Garcia-Rill, Skinner and Gilmore, 1981; Garcia-Rill, Skinner, Jackson and Smith, 1983; Garcia-Rill, 1986). It has been found that to initiate gait in decerebrate cats walking on a treadmill using MLR stimulation, the ventral-lateral quadrant of the spinal cord must be intact (Steeves and Jordan, 1980). The descending tract that appears the most likely to carry this initiation signal is the reticulospinal pathway. It is possible that inadequate activation of the MLR, due to disturbed input to it from the PPN, whose activation has been disrupted by improper input from the globus pallidus, may result in the inability to initiate walking during freezing episodes in PD patients. It should be noted however that these results were found in decerebrate cats, in which cortical involvement is removed. Interestingly, it was reported by Nathan (1994) that in 44 humans who had undergone incomplete cordotomies to combat extreme pain due to cancer, severe mobility problems were only seen in patients who had their dorso-lateral quadrants, where the lateral cortico-spinal tract descends, cut. Here, it was seen that cutting through the anterior half of the cut at any thoracic level did not disturb their walking. However, the further the cut was made into the posterior quadrants, the more deficits occur. Still, cutting of one of the posterior quadrants was not enough to prevent mobility. It was only in the case of cutting the lateral corticospinal tract completely, and 85-90% of the contralateral corticospinal tract that complete paralysis was seen. This eventually recovered enough that in two months, the patient was walking, though with severe spastic paraparesis. As such, it appears that several descending tracts can be removed without major gait difficulties occurring. The lateral corticospinal tract seems to be one of the few tracts necessary to get relatively normal gait in humans.

This fact, in combination with the effect that the amount of attention given to the task can affect the step cycle, indicate that how the basal ganglia interact with the motor cortex and the corticospinal tract needs to be examined. The globus pallidus sends afferent to the ventro-lateral thalamus, which then outputs to the supplementary motor area (SMA) (Schell and Strick, 1984). The SMA has connections to and can influence the output of the primary motor cortex. As well, the SMA has direct connections to the cervical and lumbar regions of the spinal cord itself (Dum and Strick, 1991; He, Dum and Strick, 1995). The activity of the SMA, which is involved in the control of internally generated movements, is decreased in PD patients when compared to normals (Bereitschaftspotential (BP) amplitude reduced: Dick, Rothwell, Day, Cantello, Buruma, Gioux, Benecke, Berardelli, Thompson, and Marsden, 1989; PET: Playford, Jenkins, Passingham, Nutt, Frankowiak, and Brooks, 1992; PET and BP: Jahanshahi, Jenkins, Brown, Marsden, Passingham, and Brooks, 1995; MRI - specifically the rostral SMA: Sabatini, Boulanouar, Fabre, Martin, Carel, Colonnese, Bozzao, Berry, Montastruc, Chollet and Rascol, 2000). During gait, a SPECT study also showed decreased activity of the rostal portion of the SMA during walking on a treadmill in PD patients compared to normal (Hanakawa, Katsumi, Fukuyama, Honda, Hayashi, Kimura, and Shibasaki, 1999). This rostal part of the SMA seems to be more involved with complex motor behaviour than simple movements (Picard and Strick, 1996). Meanwhile, the patients seem to use the premotor cortex, which is used during external cued movements, to help guide their movements (PET: Samuel, Ceballos-Baumann, Blin, Uema, Boecker, Passingham and Brooks, 1997; MRI: Sabatini et al., 2000). When investigating the activation of the cortex during gait, it was found that during paradoxical gait, there was significantly enhanced activation of the premotor cortex when visual guides (specifically, transverse lines across the walkway) were used to help aid in walking (Hanakawa, Fukuyama, Karsumi, Honda and Shibasaki, 1999). These results indicate that PD patients have a much more difficult time in initiating internally self-generated movements, but they can utilize external cueing to activate another pathway though the premotor cortex to start the process of movement. If this is the case, it may be that conducting these experiments while walking on the treadmill might have prevented some freezing episodes that the patients might have normally undergone. The sound of the treadmill and the sensation of the ground moving beneath the PD patients' feet might have been enough to be used as a source of external cueing. It is advisable that for future studies during gait with PD patients that overground locomotion is considered.

In addition to the changes in output of the SMA and PMC with PD, there also appears to be changes in how proprioceptive somatosensory input is processed at higher levels in the CNS. Several studies have shown that kinesthetic information from the periphery is used inaccurately in PD (Klockgether, Borutta, Rapp, Spicker, and Dichgans, 1995; Demerci, Grill, McShane and Hallett, 1997; Jobst, Melnick, Byl, Dowling and Aminoff, 1997; Rickards and Cody, 1997). All these studies examined how movements of the upper limbs were inaccurately assessed when only proprioceptive input was available to the PD patients. When visual information was supplied, patients were able to accurately assess the movement their limbs had undergone (Klockgether et al., 1995; Demerci et al., 1997; Jobst et al., 1997). Examining the activity of the somatosensory primary cortex using PET scanning techniques has been done by applying a vibratory stimulus to a mobilized metacarpal joint in the index figure of both patients and non-neurologically impaired controls. It was found that with the passive stimulation, there was decreased activation in the contralateral primary sensory cortex, secondary sensory cortex, lateral premotor cortex, posterior cingulate gyrus, and basal ganglia in the patients when compared to the controls. There was also a decrease in activity bilaterally in the prefrontal cortex (Brodmann area 10). Interestingly, there was a relative increase in activity in the ipsilateral primary and secondary sensory cortex and the insular cortex in the patients (Boecker, Ceballos-Baumann, Bartenstein, Weindl, Siebner, Fassbender, Munz, Schwaiger and Conrad, 1999). Sensory processing has also been investigated using sensory evoked potentials (SEP's) from the tibial nerve in the leg to the cortex (P37-N50 responses) in both patients and controls. It was found the SEP's were either absent or greatly reduced in amplitude in akinetic-rigid PD patients when compared to the SEP's evoked in control subjects with the same stimulation (Tinazzi, Fiaschi, Idone, Tezzon, and Zanette, 1999).

Attentional Difficulties in Parkinson's Disease:

It is known that PD patients have greater difficulties in doing two or more tasks that require attention simultaneously than normal age-matched adults do (Brown and Marsden, 1988; Dalrymple-Alford, Kalders, Jones and Watson, 1994). The tasks in the Brown and Marsden study involved two verbally oriented tasks, while the tasks used by Dalrymple-Alford and colleagues used a visual-spatial motor task and a verbal task. Still, both sets of tasks were ones that were considered "voluntary" and thus required attention. Walking is generally considered an automatic task. It could be assumed that it would not require a lot of attentional control. Still, studies done in older normal adults indicate that postural control during stationary stance and walking requires a greater proportional of attentional resources than seen with younger adults (Teasdale, Bard, LaRue and Fleury, 1993; Lajoie, Teasdale, Bard and Fleury, 1996). It may that that with impairment of the SMA, and therefore the problem with generating internally activated movements, the PD patient has to develop conscious external cuing techniques to activate a walking pattern, requiring more conscious attention to be used during walking. When attentional demand is focussed away from the walking task, the gait pattern becomes more distorted from the normal.

It is interesting to note that this requirement for attention on walking is also seen in incomplete spinal cord injured patients who regain some walking ability (Lajoie, Barbeau and Hamelin, 1999). During sitting and standing, when an auditory stimulus was given that both the patients and a control group had to give a verbal response to, the patients had faster reaction times than the control subjects. However, when walking at preferred speed, the patients' reaction times to responding to the cue was much slower than the controls'. The patients had been instructed to consider walking as the primary task and responding to the cues as the secondary task. A differential effect was found when comparing their reaction times if the cue was given during single or double support, with the reaction times being slower during single support phases as opposed to during double support. This differential effect was not seen in the control subjects. The fact that the patients were slower in responding while walking indicated that this task is cognitively challenging to them and requires some attentional demand. Therefore, it appears that both traumatic injuries and chronic neuropathologies may require the walking task to become more dependent on supraspinal input.

Descending Influences on the Group Ib Reflex Arc and Interneurons:

How is this relevant to the reflex arc investigated in this study? It is known that activity within the Ib interneuron can be modulated by a variety of different inputs, including decending supraspinal input (reviewed in Jankowska, 1992). Several studies have examined how different descending systems can affect the modulation of the Ib afferent reflex arc in the static state. Eccles and Lundberg (1959) tested the magnitude of the effect of a variety of conditioning stimuli on the H-reflexes of several muscles in cats that were first decerebrated and then spinalized. They also did intracellular recording from a variety of the motorneurons being examined with the conditioning stimuli in both the decerebrate and spinalized preparations. They generally found that in the decerebrate state, there was a tonic inhibition of the effects of the conditioning. This inhibitory influence was removed in the spinalized state, allowing the conditioning from a variety of different afferents to have large effects on both flexor and extensor motorneurons. This indicated that the inhibition of the conditioning effects must be due to descending input from supraspinal structures. The effects of the inhibition were more apparent in the flexors when conditioned with stimuli that were group Ib in origin. But both flexor and extensor motorneurons had descending inhibition influencing the magnitude of effects of the conditioning stimuli on the H-reflex. In investigating the level of brain stem lesion that produced the inhibitory effects, it was found that for the group 1 b reflex arc, lesioning of the brain stem at the medulla still allowed for the tonic inhibition of inhibitory reflex arc to extensors. This is different from group II and III muscle afferents, where this lesion allowed the effects of the conditioning stimulus of these afferent to be uncovered. Pontine centres were required from the tonic inhibition of these higher threshold afferents effects (Holmquist and Lundberg, 1961).

Studies were done examining the effects of the various descending systems on the motorneuron pools and interneurons affecting these motorneurons. Lundberg and Voorhoeve (1962) found that stimulation of the sensorimotor cortex in cats caused a facilitation of the synaptic actions in motorneurons of the group Ib afferents. This was seen in effects on test reflexes and through intracellular recording from the motorneurons themselves, with both inhibitory actions onto synergistic motorneurons and occasionally on the group Ib excitatory actions onto antagonistic motorneurons being found. In a concurrent study, recording from group I interneurons intracellularly showed excitatory post-synaptic potentials (EPSP's) being evoked in the interneurons when sensorimotor cortex stimulation occurred (Lundberg, Norrsell and Voorhoeve, 1962). These studies indicate that in the static state, cortical input seems to have a facilitatory effect on the interneurons in the group Ib reflex arc. Similar facilitatory effects on interneuronal pathways are seen with stimulation of the rubrospinal tract for the group Ib reflex arc. Recording intracellularly from motorneurons, a marked facilitation was seen in the reciprocal effects evoked from group Ib afferents from extensor muscles. This facilitation was seen even in the reflex pathways across joints. For example, rubrospinal facilitation allowed for Ib volleys from the toe extensor flexor digitorum longus to cause large inhibitory post-synaptic potentials (IPSP's) to be seen in the hip extensor muscles anterior biceps and semimembranosus and adductor femoris and longus. Therefore, the group Ib effects are facilitated over a wide distribution of the motorneuronal pools. There were also facilitation of group Ib effects seen with rubrospinal stimulation in inhibitory pathways from extensors to flexor nuclei and flexor to extensor nuclei, as well as excitatory pathways from flexors to extensor nuclei (Hongo, Jankowska and Lundberg, 1969). A subsequent study by the same authors investigated the effects of the rubrospinal stimulation on the interneurons themselves (Hongo, Jankowska and Lundberg, 1972). They found for interneurons that were activated by group I afferent stimulation, 2 groups of cells received monosynaptic excitatory action from the rubrospinal tracts. These were a) interneurons that received monosynaptic group I EPSP's and b) interneurons receiving disynaptic group I IPSP's. The authors note that some of the cells probably receive input from group Ia afferents, some from group Ib and some from both types of afferents. In the opposite manner, an inhibition of transmission from group Ib afferents to hindlimb motorneurons is seen with dorsal reticospinal activation (Engberg, Lundberg and Ryall, 1968), which the authors concluded was due to an inhibition at the interneuronal level. This inhibition of the reflex pathways was seen for both inhibitory actions of an extensor onto a synergistic extensor (ie. quadriceps afferent stimulation onto gastrocnemius-soleus motorneuron) and excitatory actions of an extensor onto a flexor motorneuron. Therefore, at least in the static state, there are a number of different descending pathways that act with different effects on the group Ib interneuron and the resultant reflex arc.

The fact that these connections exist does allow for the hypothesis that changes in the descending input during walking in PD patients can affect how the reflex arc may be modulated. More work is needed to prove this concept. To fully investigate it, recordings would have to be done at the motorneuronal and interneuronal level in a model that accurately represents how the complex interactions of the different components of the nervous system utilized in the production of walking are modified with PD.

Summary:

As a consequence of the variety of difficulties PD produces in people that suffer from it, the results of this study are not very clear. The symptom of an inability to initiate a step was initially hypothesized to be partially due to a modification in the group I reflex pathway, which appears to be instrumental in the stance-to-swing transition. This might still be true. There was a distinct difference found in how young healthy adults and PD patients modulate the group Ib reflex arc during sitting. However, in both groups, during walking the conditioned H-reflex did not significantly differ in magnitude from the control reflex. As well, tibial nerve train stimulation at an intensity that would activate the group I afferents did not cause any major change in the durations of the step cycle or its phases. These results might indicate that while walking in a posturally stable environment, this afferent input will not have a huge effect on the magnitude of activity of the soleus motorneurons or on the duration of this muscle's activity. However, when considering "freezing", there are several other factors that could be of equal or greater consequence in the development of this symptom. These could include the requirement for attention during locomotion and the fact that somatosensory afferent processing seems to be impaired in these patients at higher levels of the cortex. As well, the reduction in activity of the SMA in voluntary movements, which is implicated in the control of internally generated movements, and the increased in activity of the premotor cortex, indicating a greater reliance on external cueing, may also contribute to the changes in the gait pattern.

One problem that needs to be addressed is the fact that this study was done using treadmill walking. At least one of the patients demonstrated freezing with overground walking that did not occur while walking on the treadmill. Other patients, while not showing the extreme problems with freezing that this patient showed, had difficulties with turning while walking overground. None of these difficulties could be seen with walking on the treadmill. The sensory input from the treadmill, such as the constant movement of the belt backwards, forcing the patient to take a step to remain in place, or the constant auditory sound produced by the treadmill's motor, may have been enough of a sensory cue to produce a consistent gait pattern. As such, more definite results might have been found if the subjects could be tested while walking overground. The ideas and problems listed above need to be considered for future studies examining the difficulties in walking these patients suffer from.

5.5 REFERENCES:

Aminoff M.J., Siedenburg R., and Goodin D.S., 1997. Changes in forearm EMG and cerebral evoked potentials following sudden muscle stretch during isometric contractions in patients with Parkinson's disease. *Brain Res. 757*: 254-259.

Andrews C., 1973. Influence of dystonia on the response to long-term L-dopa therapy in Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry 36*: 630-636.

Boecker H., Ceballos-Baumann A., Bartenstein P., Weindl A., Siebner H.R., Fassbender T., Munz F., Schwaiger M., and Conrad B., 1999. Sensory processing in Parkinson's and Huntington's disease: Investigations with 3D $H_2{}^{15}0$-PET. *Brain 122*: 1651-1665.

Brown R.G. and Marsden C.D., 1988. Internal versus external cues and the control of attention in Parkinson's disease. *Brain 111*: 323-345.

Burleigh-Jacobs A., Horak F.B., Nutt J.G. and Obeso J.A., 1997. Step initiation in Parkinson's disease: influence of levodopa and external sensory triggers. *Movement Disorders 12*(2): 206-215.

Capaday C., Lavoie B.A., Barbeau H., Schneider C. and Bonnard M., 1999. Studies on the corticospinal control of human walking. I. Responses to focal transcranial magnetic stimulation of the motor cortex. *J. Neurophysiol. 81*: 129-139.

Dalrymple-Alford J.C., Kalders A.S., Jones R.D. and Watson R.W., 1994. A central executive deficit in patients with Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry 57*: 360-367.

Delwaide P.J. and Oliver E., 1988. Short-latency autogenic inhibition (IB inhibition) in human spasticity. *J. Neurol. Neurosurg. Psychiatry 51*: 1546-1550.

Delwaide P.J., Pepin J.L. and Maertens de Noordhout A., 1991. Short-latency autogenic inhibition in patients with parkinsonian rigidity. *Ann. Neurol. 30*: 83-89.

Demirci M., Grill S., McShane L and Hallett M., 1997. A mismatch between kinesthetic and visual perception in Parkinson's disease. *Ann. Neurol. 41*: 781-788.

Dick J.P.R., Rothwell J.C., Day B.L., Cantello R., Buruma O., Gioux M., Benecke R., Berardelli A., Thompson P.D. and Marsden, C.D., 1989. The Bereitschaftspotential is abnormal in Parkinson's disease. *Brain 112*: 233-244.

Dietz V. and Colombo G., 1998. Influence of body load on the gait pattern in Parkinson's disease. *Movement Disorders 13*(2): 255-261.

Downes L., Ashby P., and Bugaresti J., 1995. Reflex effects from Golgi tendon organ (Ib) afferents are unchanged after spinal cord lesions in humans. *Neurol. 45*: 1720-1724.

Dum R. P. and Strick P.L., 1991. The origin of corticospinal projections from the premotor areas in the frontal lobe. *J. Neurosci. 11*(3): 667-689.

Duysens J. and Pearson K.G., 1980. Inhibition of flexor burst generation by loading ankle extensor muscles in walking cats. *Brain Res. 187*: 321-332.

Eccles R.M. and Lundberg A., 1959. Supraspinal control of interneurones mediating spinal reflexes. *J. Physiol. 147*: 565-584.

Engberg I., Lundberg A., and Ryall R.W., 1968. Reticulospinal inhibition of transmission in reflex pathways. *J. Physiol, 194*: 201-223.

Fahn S., Elton R.L. and members of the UPDRS Development Committee, 1987. Unified Parkinson's disease rating scale. In: *Recent Developments in Parkinson's Disease Volume II.* (eds.) Fahn S., Marsden C.D., Goldstein M. and Calne C.D. Macmillan, New York. pp. 153-163.

Fahn S., 1995. The freezing phenomenon in parkinsonism. In: *Advances in Neurology Vol. 67: Negative Motor Phenomena.* (eds.) Fahn S., Hallett M., Luders O. and Marsden C.D. Lippincott-Raven Publishers, Philadelphia. pp. 53-63.

Forssberg H., Johnels B. and Steg G., 1984. Is parkinsonian gait caused by a regression to an immature walking pattern. *Advances in Neurology, Vol. 40.* (eds.) Hassler R.G. and Christ J.F. Raven Press, New York. pp. 374-379.

Garcia-Rill E., Skinner R.D. and Gillmore S.A., 1981. Pallidal projections to the mesencephalic locomotor region (MLR) in the cat. *Amer. J. of Anat. 161*, 311-321.

Garcia-Rill E., Skinner R.D., Jackson M.B. and Smith M.M., 1983. Connections of the mesencephalic locomotor region (MLR) I. substantia nigra afferents. *Brain Res. Bull. 10*(1): 57-62.

Garcia-Rill E., 1986. The basal ganglia and the locomotor region. *Brain Res. Reviews 11*: 47-63.

Giladi N., Kao R., and Fahn S., 1997. Freezing phenomenon in patients with parkinsonian syndromes. *Movement Disorders 12*(3): 302-305.

Giladi N., McMahon D., Przedborski S., Flaster E., Guillory S, Kostic V., and Fahn, S., 1992. Motor blocks in Parkinson's disease. *Neurology 42*: 333-339.

Goetz C.G., Stebbins G.T., Chmura T.A., Fahn S., Klawans H.L. and Marsden D., 1995. Teaching tape for the motor section of the unified Parkinson's disease rating scale. *Movement Disorders 10*(3): 263-266.

Guertin P., Angel M.J., Perreault M.-C. and McCrea D.A., 1995. Ankle extensor group I afferents excite extensors throughout the hindlimb during fictive locomotion in the cat. *J. Physiol. 487*(1): 197-209.

Hammerstad J.P., Elliot K., Mak E., Schulzer M., Calne S. and Calne D.B., 1994. Tendon jerks in Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry [P-D Sect.] 8*: 123-130.

Hanakawa T., Fukuyama H., Katsumi Y., Honda M., and Shibasaki H., 1999. Enhanced lateral premotor activity during paradoxical gait in Parkinson's disease. *Ann. Neurol. 45*: 329-336.

Hanakawa T., Katsumi Y., Fukuyama H., Honda M., Hayashi T., Kimura J. and Shibasaki H., 1999. Mechanisms underlying gait disturbance in Parkinson's disease – a single photo emission computed tomography study. *Brain 122*: 1271-1282.

He S.-Q., Dum R.P. and Strick P.L., 1995. Topographic organization of corticospinal projections from the frontal lobe: motor areas on the medial surface of the hemisphere. *J. Neurosci. 15*(5): 3284-3308.

Holmquist B. and Lundberg A., 1961. Differential supraspinal control of synaptic actions evoked by volleys in the flexion reflex afferents in alpha motorneurones. *Acta Physiol. Scand. Vol. 54, Suppl. 186*: 1-51.

Hongo T., Jankowska E. and Lundberg A., 1969. The rubrospinal tract. II. Facilitation of interneuronal transmission in reflex paths to motorneurones. *Exp. Brain. Res. 7*: 365-391.

Hongo T., Jankowska E. and Lundberg A., 1972. The rubrospinal tract. IV. Effects on interneurones. *Exp. Brain Res. 15*: 54-78.

Hoehn M.M and Yahr M.D., 1967. Parkinsonism: onset, progression, and mortality. *Neurology 17*(5): 427-442.

Jahanshahi M., Jenkins I.H., Brown R.G., Marsden C.D., Passingham R.E., and Brooks D.J., 1995. Self-initiated versus externally triggered movements: I. An investigation using measurement of regional cerebral blood flow with PET and movement-related potentials in normal and Parkinson's disease subjects. *Brain 118*: 913-933.

Jankowska E., 1992. Interneuronal relay in spinal pathways from proprioceptors. *Progress in Neurobiology 38*: 335-378.

Jobst E.E, Melnick M.E., Byl N.N., Dowling G.A., and Aminoff M.J., 1997. Sensory perception in Parkinson's disease. *Arch. Neurol. 54*: 450-454.

Klockgether T., Borutta M., Rapp H., Spieker S., and Dichgans J., 1995. A defect in kinesthesia in Parkinson's disease. *Movement Disorders 10*(4): 460-465.

Lajoie Y., Barbeau H. and Hamelin M., 1999. Attentional requirements of walking in spinal cord injured patients compared to normal subjects. *Spinal Cord 37*: 245-250.

Lajoie Y., Teasdale N., Bard C., and Fleury M., 1996. Upright stance and gait: Are there changes in attentional requirements related to normal aging? *Exp. Aging Res. 22*: 185-198.

Lundberg A., Norrsell U., and Voorhoeve P., 1962. Pyramidal effects on lumbo-sacral interneurones activated by somatic afferents. *Acta Physiol. Scand. 56*: 220-229.

Lundberg A. and Voorhoeve P., 1962. Effects from the pyramidal tract on spinal reflex arcs. *Acta Physiol. Scand. 56*: 201-219.

Martin J.P., 1967. Locomotion and the basal ganglia. In: *The Basal Ganglia and Posture.* Pitman Medical Publishing Co. Ltd. London. pp. 20-35.

Martinelli P. and Mantagna P., 1979. Conditioning of the H-reflex by stimulation of the posterior tibial nerve in Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry 42*: 701-704.

McLeod J.G. and Walsh J.C., 1972. H-reflex studies in patients with Parkinson's disease. *J. Neurol. Neurosurg. Psychiatry 35*: 77-80.

Morris M.E., Iansek R., Matyas T.A. and Summer J.J., 1994. The pathogenesis of gait hypokinesia in Parkinson's disease. *Brain 117*: 1169-1181.

Morris M.E., Iansek R., Matyas T.A. and Summer J.J., 1996. Stride length regulation in Parkinson's disease: normalization strategies and underlying mechanisms. *Brain 119*: 551-568.

Nathan P.W., 1994. Effects on movement of surgical incisions into the human spinal cord. *Brain 117*: 337-346.

Pedersen S.W., Eriksson T. and Oberg B., 1991. Effects of withdrawal of antiparkinson medication on gait and clincal score in the Parkinson patient. *Acta Neurol. Scand. 84*: 7-13.

Picard N. and Strick P.L., 1996. Motor areas of the medial wall: a review of their location and functional activation. *Cerebral Cortex 6*: 342-353.

Pierrot-Deseilligny E., Bergego C., and Mazieres L., 1983. Reflex control of bipedal gait in man. In: *Motor Control Mechanisms in Health and Disease,* (ed.) Desmedt J.E. Raven Press, New York. pp. 699-716.

Pierrot-Deseilligny E., Katz R. and Morin C., 1979. Evidence for Ib inhibition in human subjects. *Brain Res. 166*: 176-179.

Playford E.D., Jenkins I.H., Passingham R.E., Nutt J., Frackowiak R.S.J. and Brooks D.J., 1992. Impaired mesial frontal and putamen activation in Parkinson's disease: a positron emission tomography study. *Ann. Neurol. 32*: 151-161.

Rickards C. and Cody F.W.J., 1997. Proprioceptive control of wrist movements in Parkinson's disease: Reduced muscle vibration-induced errors. *Brain 120*: 977-990.

Sabatini U., Boulanouar K, Fabre N., Martin F., Carel C., Colonnese C., Bozzao L., Berry I., Montastruc J.L., Chollet F., and Rascol O., 2000. Cortical motor reorganization in akinetic patients with Parkinson's disease – a functional MRI study. *Brain 123*: 394-403.

Samuel M., Ceballos-Baumann A.O., Blin J., Uema T., Boecker H., Passingham R.E., and Brooks D.J., 1997. Evidence for lateral premotor and parietal overactivity in Parkinson's disease during sequential and bimanual movements – a PET study. *Brain 120*: 963-976.

Schell G.R. and Strick P.L., 1984. The origin of thalamic inputs to the arcuate premotor and supplementary motor areas. *J. Neurosci. 4*(2): 539-560.

Schubert M., Curt A., Jensen L., and Dietz V., 1997. Corticospinal input in human gait: modulation of magnetically evoked motor responses. *Exp. Brain Res. 115*: 234-246.

Steeves J.D. and Jordan L.M., 1980. Localization of a descending pathway in the spinal cord which is necessary for controlled treadmill locomotion. *Neurosci. Let. 20*: 283-288.

Stephens, M.J. and Yang, J.F., 1996. Short latency, non-reciprocal group I inhibition is reduced during the stance phase of walking in humans. *Brain Research 743*: 24-31.

Tatton W.G. and Lee R.G., 1975. Evidence for abnormal long loop reflexes in rigid Parkinsonian patients. *Brain Res. 100*(3): 671-676.

Teasdale N., Bard C., LaRue J. and Fleury M., 1993. On the cognitive penetrability of posture control. *Exp. Aging Res. 19*: 1-13.

Tinazzi M., Fiaschi A., Idone D., Tezzon F., and Zanette G., 1999. Parkinson's disease and lower limb somatosensory evoked potentials: Apomorphine-induced relief of the akinetic-rigid syndrome and vertex P37-N50 potentials. *J. Neurol. Sci. 164*: 163-171.

Yanagiasawa N., Ueno E., and Takami M., 1991. Frozen gait of Parkinson's disease and vascular parkinsonism – a study with floor reaction forces and EMG. *Neurobiological Basis of Human Locomotion.* (eds.) Shimamura M., Grillner S., and Edgerton V.R. Japanese Scientific Societies Press. Tokyo. pp. 291-304.

Zehr EP, Stein RB, Komiyama T, Kenwell Z, 1995. Linearization of force sensing resistors (FSR's) for force measurement during gait. *Proc. 17th Ann. International Conf. IEEE Engineering in Medicine and Biology Soc*, pp.300-301.

6.0: CONCLUSIONS:

This thesis examined the role of load information in the regulation of the patterning of the step cycle (both in terms of amplitude of muscle activation and durations of the phases of the step cycle). Specifically, it examined the effects of load on the stance-to-swing transition. Previous work done in a number of reduced animal preparations had indicated that this afferent input was one of the main sources of sensory information used to dictate when this important transition would occur (See Introduction). The intent of the studies documented here was to determine how this information was used during human locomotion. Normal young adults, infants and a neuropathological patient group (people with Parkinson's disease) were studied to investigate this role. The major overall conclusion of the projects discussed in this thesis is that information about the amount of load placed on the extensor muscles of the leg during human walking will affect the step cycle and its various components. However, the step cycle is affected in different ways depending upon the preparation being examined. As well, the modulation of the group I disynaptic reflex arc is task dependent as it is modified between quiescent static and walking tasks. In addition, impaired descending input from the supraspinal centers can also affect the modulation of this reflex arc, at least in the quiescent case, as seen in people with Parkinson's disease (PD). It is possible that the modulation of this reflex may also be modified during the locomotor task, which may contribute to the gait difficulties seen in these patients. However, the preliminary results so far are inconclusive.

Main Findings of this Thesis:

There are 4 main findings of this thesis. First,

1. The inhibition of the soleus H-reflex found with prior MG stimulus conditioning at disynaptic latencies found in quiescent sitting by Pierrot-Deseilligny and colleagues (1979, 1981) is not found in all subjects. During walking, the inhibition is reduced and in a small subset of the subjects, is found to switch to a facilitation of the reflex.
2. In a posturally stable situation, changes in the amount of load being carried by the extensor muscles during stance result in relatively little change in the duration of the muscle activity or the step cycle durations. To compensate for the change in load, the amplitude of the extensor EMG activity is modified. However, when postural instability is introduced as well as the increase in load, the durations of the extensor EMG activity and the step cycle and stance phase durations are prolonged. This indicates that the response to load changes is dependent on the postural situation introduced with the load change. As well, the modulations of the amplitude and the duration of the muscle activity can be controlled separately.
3. When load is applied to non-independently locomoting infants walking on a treadmill, regardless of how the load is applied, the response is a prolongation of the stance phase of the step cycle, which is also seen in reduced animal preparations. Evidence suggests that the connections from the supra-spinal centers, particularly the cortico-spinal tract, are not fully mature in these infants. As a result, it appears that the ability to modulate the response to different situations is dependent on an intact spinal system.

4. Parkinsonian patients, who have difficulties initiating the stance-to-swing transition, do not exhibit the inhibition of the soleus H-reflex with prior MG nerve conditioning at disynaptic latencies in sitting. There is a trend towards facilitation, though it is not significant. This is generally in agreement with the findings of Delwaide and colleagues (1991). However, they also do not exhibit a clear inhibition or facilitation of the reflex during walking. As well, stimulation of the tibial nerve with a train of pulses at the end of swing has very little effect on the timing of the phases of the step cycle. However, this was tested while the subjects were walking on a treadmill and attending to the walking task. It was found that when attention is distracted from the walking task, the gait pattern of the Parkinsonian subject could change substantially. More work needs to be done with the task of attention-distracted walking to see how the results may differ in this scenario.

Activation of Group I afferents in both Normal Adult and Parkinsonian Gait:

In Chapters 2 and 5, the modulation of the disynaptic group I afferent reflex arc, specifically the group Ib, was examined under the different tasks of quiet sitting and walking in non-neurologically impaired and Parkinsonian (PD) subjects. It had been shown in a number of previous studies that reflex modulation can be task dependent in humans (Stein and Capaday, 1987) and animals (Prochazka, 1989). Previous work in humans had also shown that the group Ib disynaptic reflex arc appeared to be modulated differently between normal adults and PD subjects (compare Pierrot-Deseilligny, Katz and Morin, 1979 to Delwaide, Pepin and Maertens de Noordhout, 1991). In young healthy adults, we were able to replicate the results of Pierrot-

Deseilligny and colleagues (1979, 1981) during quiet sitting to an extent. In the 15 subjects studied (Chapter 2), we were only able to find a significant inhibition in the magnitude of the soleus H-reflex with a conditioning stimulation of the afferents from the medial gastrocnemius nerve at disynaptic latencies in two thirds of the subjects during quiet sitting. Even when the conditioning stimulus consisted of up to 4 pulses below motor threshold to the MG nerve, which would have a cumulative effect on the soleus motorneurons (Gossard, Brownstone, Barajon and Hultborn, 1994), 5 subjects did not show a significant inhibition of the soleus H-reflex with the conditioning stimulation. This may indicate that in the intact system, with all the other afferent and descending inputs onto the soleus motorneurons, the activation of the group I afferents from the MG nerve did not have enough synaptic efficacy to affect output of the soleus motorneurons to the tibial nerve stimulation. It is known from animal work that the inputs from afferents from different muscles can have differing magnitudes of effect on the motorneuronal pool of other muscles (Whelan, Hiebert and Pearson, 1995). It may be that in the scenario studied the group I afferent output of the MG muscle does not have large effects on the output of the soleus motorneuronal pool. There is also the possibility that there might be excitation of the motorneuronal pool through group Ia disynaptic pathways.

We were also able to replicate the results of Delwaide and colleagues on the effect of the conditioning stimulation during quiet sitting in PD patients. Here, there is a movement away from the inhibition of the soleus H-reflex with a conditioning MG stimulation at disynaptic latencies. The trend is towards a facilitation of this reflex, though no statistically significant difference was seen between the control and conditioned H-reflex magnitudes. However, at all 3 condition-test intervals studied, there was a significant difference between the results collected from the PD patients and the results from the normal subjects. This indicates that in the neurologically impaired system of the PD patient, the way this reflex arc is modulated is different from non-neurologically impaired young adults.

There are distinct differences in how the reflex arc is modulated during quiet sitting and during walking in normal subjects. There is a significant reduction in the magnitude of the inhibition in the soleus H-reflex with conditioning stimulation. While background contraction of the soleus muscle contributes to the reduction in inhibition, it cannot account for all of the reduction seen during walking (Chapter #2). Thus, a task-dependent change in the modulation of this particular reflex arc does occur. In the pooled data, a clear reflex-reversal from inhibition in sitting to facilitation in walking is not seen. This possible facilitation had been hypothesized based on the previous studies done on reduced animal preparations. However, some subjects (4 of 10) did show a significant facilitation of the H-reflex magnitude with the conditioning stimulation during walking (Figure 2.5). These results may indicate that during walking, the inhibitory group Ib interneurons are not excited during the task, and that the excitatory group Ib interneurons are activated. However, in some subjects, these excitatory effects when combined with the other afferent inputs do not cause a sufficient increase in motorneuron excitability to generate an increase in the H-reflex magnitude. It is interesting to note a recent study has found that synaptic transmission of group I, group II and cutaneous afferent input is reduced (to approximately 80% of control) in an MLR-stimulation-induced fictive locomotor preparation compared to when the animal was not producing a locomotor pattern (Perreault, Shefchyk, Jimenez and McCrea, 1999). This effect was uncovered by monitoring the monosynaptic extracellular field potentials evoked by electrical stimulation of ipsilateral hindlimb nerves carrying these afferents. In light of these results, it would appear that afferent input would not have the same magnitude of effect as when applied during the non-locomoting state. If and to what extent this reduction in the transmission of afferent information affects the locomotor pattern of an intact system, whether quadrupedal or bipedal, is not known. However, if a reduction in the synaptic transmission of afferent input occurs during walking, it may indicate that increased afferent input from the periphery (ie an increase in postural instability occurring during walking) is required to produce enough of an effect on the motorneuronal pools to cause a change in the locomotor pattern.

In the PD patients, there was no statistically significant difference in the magnitudes of the H-reflexes generated with or without a conditioning stimulus. Also, no significant difference was seen between the results of the medial gastrocnemius afferent stimulation on the magnitude of the soleus H-reflex collected during sitting and walking at condition-test intervals corresponding to a disynaptic pathway. There was a slight trend of the H-reflex being inhibited during walking with the conditioning stimulus, when the trend was towards facilitation during quiet sitting. However, there were only 5 subjects in which data was collected in both conditions and the results from more subjects are required to determine if this trend is consistent.

A possibility as to why the group Ib afferents do not appear to have large effects on the output of the soleus motorneuronal pool in walking in PD patients may be due to that fact that walking may not be as automatic a task in these patients. From the results of the distraction task, it would appear that supraspinal input does have an effect on the pattern generated from walking in these patients. This change in supraspinal input may affect the activity of the various interneurons found in the spinal cord. Perhaps the afferent input from the periphery is "gated" further in these patients. From other research, it is known that the motor cortex seems to have a greater effect on the flexors than the extensors during walking (Capaday, Lavoie, Barbeau, Schneider and Bonnard, 1999; Schubert, Curt, Jensen and Dietz, 1997). An impaired signal from the motor cortex may result in both the flat foot contact and loss of the second TA EMG burst associated with the control of lowering the foot after heel contact. More "conscious" control, with increased attentional demand, appears to be necessary for the PD patients to generate a step cycle pattern that approximates the normal.

Possible Problems with Protocol:

A possible area of concern with this type of study is with the methodology. The H-reflex as a control reflex has been used in a number of different studies that want to examine the role of different afferent inputs on the motor output of the spinal cord. However, in using it to examine the group Ib reflex, a number of difficulties were encountered. One, the range of H-reflex magnitudes that the testing was done in (10-15% M-maximum) was along the steepest part of the H-reflex magnitude gain curve (Taborikova and Sax, 1968: Crone, Hultborn, Mazieres, Morin, Nielsen and Pierrot-Deseilligny, 1990). This meant that the slightest change in input could result in large changes in the variability of the H-reflex generated. This effect was controlled for by only including trials of control H-reflexes where the variability was less than 20% of the average H-reflex size being generated. However, considering the relatively modest size of the inhibition generated (on average, approximately 10%), this was an area of concern. It became an even greater concern during the walking trials. To maintain the reflex within the accepted variability range, the number of control and conditioned stimuli had to be doubled within a given trial. This meant longer times walking on the treadmill. While not a concern with the young adult subjects, the PD patients could not walk on the treadmill for long periods of time. While adequate rest periods were given between trials, the number of trials and length of the test session was a factor that had to be considered in selecting what could be examined in any given session.

There is also a possible concern with the amount of time between each tibial nerve stimulus. We allowed a consistent three-second interval between the stimuli during the static task. Work by Taborikova and Sax (1969) has shown that a given H-reflex has not recovered maximum peak-to-peak amplitude until 7-10 seconds after the previous stimulus. However, leaving that long a time between stimuli would have greatly prolonged the trials. Given that we were consistent with the interval duration, the H-reflex should have recovered the same amount in the given time. Thus, we were confident that shortening the inter-stimulus interval was not an extensive problem. But again, it is a factor that has to be considered when conducting these types of studies.

As well, this protocol only activates one set of muscle afferents from one muscle, which may not have a large effect on the motorneuronal pool of the muscle that the control reflex is being generated in. With all the other afferent and descending inputs onto the motorneurons of a given muscle during walking, it may be that the effect of the single muscle afferent is not enough to produce a large effect on the reflex generated. Still, even given the above concerns, this protocol is the best possible method for examining group Ib input in the intact human in a given task.

Another possible problem with the study examining the reflex changes in PD patients is that the subjects examined might not have been severely affected enough to show a change in the modulation of the reflex arc. All the subjects were able to walk on the treadmill for 3-5 minutes at a time. Most scored a 1 on the gait portion of the UPDRS motor clinical test scale. It may be that stronger effects would be seen if the patients studied had greater severity of walking difficulties.

Future testing should also include an age-matched control group to the PD subjects. Delwaide and colleagues (1991) showed that age-matched controls do exhibit the same pattern of inhibition during sitting as seen in the young healthy subjects. However, this may differ during the walking task. It has been shown that in healthy older men, both walking speed and stride length decreased over the age of 65 years. Cycle duration times tended to be longer and more time was spent in stance as opposed to swing (Murray, Kory and Clarkson, 1969). As well, there were slight decreases in joint excursions about the hip, knee and ankle in the older men when compared with younger during walking, though the pattern of angle excursions are generally the same at different ages. Since these slight differences exist between young and older healthy adults, it is advisable to collect comparison data in the patients and age-matched controls to remove the affect of age and allow any differences found to be attributed to the disease process.

Effects of changes in load on the extensor muscles during walking in adults and infants:

In the intact adult human system, the response "chosen" to cope with the change in the amount of load being carried by the extensor muscles of the lower limb was dependent on other factors, such as the amount of postural instability the change in load caused. If the method of introducing a change in load did not cause the person to become unstable during walking, the response generated affected the amplitude of the extensor bursts, with only minor changes in the timing of the phases of the step cycle. However, if postural instability resulted with the change in load (Dietz, Quintern, Boos, and Berger, 1986; Misiaszek, Stephens, Yang and Pearson, 2000), the durations of the phases of the step cycle and the extensor bursts were prolonged to compensate and allow stability to be regained. From a biomechanical perspective, this difference in response based on the degree of postural instability introduced by the perturbation makes sense. The intact system will try to respond in the most efficient manner that allows for both stability of the body during stepping and the generation of the locomotor rhythm to be maintained. The task of walking can be broken down into two components. The first is to maintain a solid base of support underneath the body such that there is no danger of falling. The second is to generate the locomotor pattern such that forward progression of the body is possible. These two components must be considered when "selecting" the response to a given perturbation. In the case of changing the load on the extensor muscles of the leg without perturbing the postural stability of the body, increased activation of the extensor muscles will generate enough force to move the body up and forward in an efficient enough manner without disrupting the locomotor cycle being generated. However, when postural stability is perturbed, regaining that stability is the most essential element. Loss of stability will result in a fall, thus halting the locomotor rhythm as well as leading to possible injury. As such, it is more efficient to utilize a response that will allow stability to be maintained, even if the rhythm generation must be altered to allow enough time for regaining balance.

The results of Chapter 3 were different than what had been hypothesized originally, based on the results of prior experiments on reduced animal preparations (see Duysens, Clarac and Cruse, 2000 for review). In the reduced preparations, the response to the change in load afferent input, whether introduced via mechanical or electrical means, was to change the durations of the extensor bursts, with corresponding changes to the durations of the stance phase and step cycle. To investigate whether the differences found in the responses were due to the differences between the species studied (quadrupedal walking vs. bipedal walking) or the preparation studied (fictive, spinalized, decerebrate or intact nervous system), the effect of load was investigated in the infant stepping reflex model (Chapter 4). This model was selected since the descending inputs from the supraspinal centers (particularly the corticospinal tract) are not fully mature. As a result, it resembled to a certain extent the spinalized animal preparation. When increasing the amount of load placed on the stance leg either directly (though vertical application of load down during the stance phase), or indirectly (by halting the progression of the contralateral swing limb), the infants responded in the same manner, similar to the responses of the reduced animal preparations. There was a consistent prolongation of the extensor burst with increased load, regardless of how it was applied. This is different than when these two methods of applying load were studied in the adult (Chapter 3 for direct application of load, a posturally stable situation, versus Dietz et al., 1986 for indirect, which is posturally unstable). It therefore appears the ability to modify the response to a change in load given a certain situation is dependent on a fully mature intact system. It should be noted that as the infant model is not posturally stable (none of the infants studied were locomoting independently), the response generated was not used to maintain postural stability. It appears to be only when supraspinal input is mature that a variety of responses to a given perturbation are possible. Thus, it is the degree of functional completeness of the nervous system as opposed to the different species that account for the differences in responses seen.

In considering the role of corticospinal input on locomotion, experiments done that examine the effects of different incomplete lesions bilaterally of the dorsolateral funiculi and dorsal columns of the spinal cord in cats indicate that the dorsolateral columns (the corticospinal and rubrospinal tracts) are very important in maintaining the appropriate temporal patterning of EMG activity and intralimb coordination during walking (Jiang and Drew, 1996). Lesioning of these tracts caused dragging of the paws during swing, more flexed ankle and knee joints and a disruption in the timing of hip and knee flexors. If these tracts are important in regulating the timing and coordination of joints during walking, it may explain why only one response is used to correct perturbations in the immature or reduced preparations, as the loss of descending input does not allow for modification of the response depending on the degree of instability introduced.

Concerns about the Mechanical Loading Studies:

There are a few areas of concern when comparing the results of the various mechanical loading studies. One, in comparing the results of Chapter 3 with those of Misiaszek and colleagues (2000), it should be noted that the amount of load placed on the extensor muscles was greater in the second study. The protocol in Chapter 3 either added or removed a load equivalent to 30 percent of the subject's body weight. In the study by Misiaszek's group, the amount of load added to the extensor muscles was a larger percent of the subject's body weight (approximately 60% body weight). It may be that the increase in the amount of force placed on the extensor muscles of the leg accounted for the differences in the responses seen. However, even with this increase in the amount of load added, by stabilizing the posture, the effect was seen in the amplitude of the EMG activity and not in the duration.

As well, a more quantitative method of adding load to the infants should be investigated. In the studies reported here, load was added directly by an experimenter directing force down on the hips of the infants, or indirectly by not allowing the swing leg to carry load. The amount of load could only be determined in analysis after the test session. While this is not a major concern, a more systematic method of increasing load would allow for more consistent examination of the effects of load.

General Concern of all the Studies

All the studies have one thing in common in that all the experiments were done during treadmill walking. This could be a concern as studies have shown that treadmill walking (TW) does not produce walking that is totally analogous to walking overground (OW). Stolze and his colleagues (1997) as well as Murray's group (1985) both showed that during TW, cadence becomes faster and the stride length shorter. As well, Murray and colleagues found that there was a trend towards greater muscular EMG activity during TW, though a significant increase was only seen in the quadriceps. Displacements of the head, hip and ankle were also significantly smaller in TW. The study by Stolze and colleagues showed that the change in cadence and stride length resulted in a shorter stance phase (4%), a longer swing phase (6%) and a greatly decreased time (27%) spent in double support during TW. In addition, they found a greater step width (22%) with TM walking, which seemed to be to correct for changes in postural stability. On the other hand, they found an increase in ankle rotation with TW, while Murray and colleagues found a decrease in ankle excursion. From their work, Stolze and colleagues felt that there had to be different modulation of the CPG during TW than that used in OW, though from their own study of the kinematics and EMG, Murray et al. felt that TW did not differ markedly from OW. In regards to the kinetics produced by TW compared to OW, another study showed that the vertical ground reaction forces were slightly different between the two types of walking (White, Yack, Tucker and Lin, 1998). The patterns of ground reaction forces were the same between the two modes of locomotion regardless of the speed studied (slow, normal and fast). However, it was found that there was small but significant decreases in the amplitude of the forces produced during TW in the mid- and late-stance phases during normal and fast walking speeds compared to those found during OW. In lieu of these differences, especially considering that our studies are concerned with the force generated within the extensor muscles during walking, which can be reflected by the ground reaction forces produced, there is a possibility that overground walking may produce slightly different results than those found with treadmill walking.

It could become a source of concern when testing "freezing" gait in PD patients. As outlined in the discussion of Chapter 5, these patients tend to rely on external cues to help "unfreeze" them. It is possible that in our study, using the treadmill provided enough sensory cues (either through the sound produced by the treadmill, or by the sensation of the ground moving beneath the subject's feet) to allow for the generation of a steady gait pattern. Therefore, for future studies with Parkinsonian gait, it would be advisable to use overground walking.

Future Research:

Research in the effect of load on walking, especially in infants, is continuing in Dr. Yang's lab. One project examines different disturbances and the trade-off between loading and hip angle in determining the stance-to-swing transition (Pang and Yang, in press). Another possible direction of research is a longitudinal study that examines when the ability to modulate the response generated by a change in load first emerges, and whether this emerges at a time when postural stability first develops. The infants reported here were all non-independent walkers. The walking pattern develops over several years and does not fully resemble the adult pattern until the child is approximately 7 years of age. It may be that the ability to modulate the response does not develop until the mature walking pattern emerges. Or there may be development of this ability in the human system over time, as the ability to regulate postural stability increases.

In the PD patients, further experiments are needed to systematically consider a number of the concerns that arose from these preliminary results. One, examination of the walking pattern should be done in overground walking as opposed to walking on the treadmill. This will remove the possibility of external sensory cues produced by the treadmill itself preventing the development of "freezing" during walking. Second, subjects who are more severely affected in terms of gait difficulties should be examined. Third, examination of the reflex arc while attention is diverted away from the walking task may allow for more apparent effects in the modulation of the reflex arc to be uncovered, as this will remove some of the more "conscious" control in generating the step cycle to occur.

Summary:

Load does affect the generation of the step cycle in humans. However, the manner in which changes in load are compensated for is dependent on several factors. The intact adult human system appears to have developed different strategies to counteract changes in load dependent on the degree of postural instability introduced by the load. This ability could be explained by the fact that the locomotor pattern may be modified by supraspinal input. Removal of this input may result in a single type of "hard-wired" response in the spinal circuitry being available to be utilized by the immature or reduced spinal preparation.

In terms of the impaired system of PD patients, modulation of the group I disynaptic reflex arc is different than that found in the normal subjects during quiet sitting. This change in modulation pattern is probably due to impaired descending input. However, how the reflex arc may be modulated differently from normal during walking is not clear. In both healthy young adults and PD patients, there appears to be no significant effect of the afferent conditioning stimulus on the magnitude of the H-reflex during walking. It was also found that walking is not as automatic a task in PD patients as it is in non-neurologically impaired subjects. Evidence for this is the fact that distracting conscious attention away from the walking task causes a change in the walking pattern generated. This is especially evident in the activation of the flexors. This indicates that further experiments are required to examine the effect of this reflex arc during locomotion in PD. Experiments should be done with and without distraction, to see how the impaired supraspinal input could affect the modulation of the reflex.

References:

Capaday C., Lavoie B.A., Barbeau H., Schneider C. and Bonnard M., 1999. Studies on the corticospinal control of human walking. I. Responses to focal transcranial magnetic stimulation of the motor cortex. *J. Neurophysiol. 81*: 129-139.

Crone, C., Hultborn, H., Mazieres, L., Morin, C., Nielsen, J., Pierrot-Deseilligny, E., 1990. Sensitivity of monosynaptic test reflexes to facilitation and inhibition as a function of the test reflex size: a study in man and the cat. Exp. Brain Res. 81: 35-45.

Delwaide P.J., Pepin J.L. and Maertens de Noordhout A., 1991. Short-latency autogenic inhibition in patients with parkinsonian rigidity. Ann. Neurol. 30: 83-89.

Dietz V., Quintern J., Boos G., and Berger, W., 1986. Obstruction of the swing phase during gait: phase-dependent bilateral leg muscle coordination. Brain Res. 384: 166-169.

Duysens J., Clarac F., and Cruse H., 2000. Load-regulating mechanisms in gait and posture: comparative aspects. Physiological Reviews 80(1): 83-133.

Gossard, J-P., Brownstone, R.M., Barajon, I. and Hultborn, H., 1994. Transmission in a locomotor-related group Ib pathway from hindlimb extensor muscles in the cat. Exp. Brain Res. 98: 213-228.

Jiang W. and Drew T., 1996. Effects of bilateral lesions of the dorsolateral funiculi and dorsal columns at the level of the low thoracic spinal cord on the control of locomotion in the adult cat. I. treadmill walking. *J. Neurophysiol. 76*(2): 849-866.

Misiaszek J.E., Stephens M.J., Yang J.F., and Pearson K.G., 2000. Early corrective reactions of the leg to perturbations at the torso during walking in humans. Exp. Brain Res. 131(4): 511-523.

Murray M.P., Kory R.C., and Clarkson B.H., 1969. Walking patterns in healthy old men. *J. Gerontology 24*(2): 169-178.

Murray M.P., Spurr G.B., Sepic S.B., Gardner G.M. and Mollinger L.A., 1985. Treadmill vs. floor walking: kinematics, electromyogram, and heart rate. J. Appl. Physiol. 59(1): 87-91.

Pang M.Y.C. and Yang J.F. (in press). The initiation of the swing phase in infant stepping: importance of hip position and leg loading. J. Physiol.

Perreault M.-C., Shefchyk S.J., Jimenez I., and McCrea D.A., 1999. Depression of muscle and cutaneous afferent-evoked monosynaptic field potentials during fictive locomotion in the cat. J. Physiol. 521(3): 691-703.

Pierrot-Deseilligny E., Katz R. and Morin C., 1979. Evidence for Ib inhibition in human subjects. Brain Res. 166: 176-179.

Pierrot-Deseilligny E., Morin, C., Bergego, C. and Tankov, N., 1981. Pattern of group I fibre projections from ankle flexor and extensor muscles in man. Exp. Brain Res. 42: 337-350.

Prochazka A., 1989. Sensorimotor gain control: a basic strategy of motor systems? Prog. Neurobiol. 33: 281-307.

Schubert M., Curt A., Jensen L., and Dietz V., 1997. Corticospinal input in human gait: modulation of magnetically evoked motor responses. *Exp. Brain Res. 115*: 234-246.

Stein, R.B. and Capaday, C., 1987. The modulation of human reflexes during functional motor tasks. Trends Neurosci. 11: 328-332.

Stolze J., Kuhtz-Buschbeck J.P., Mondwurf C., Boczek-Funcke A., Johnk K., Deuschl G. and Illert M., 1997. Gait analysis during treadmill and overground locomotion in children and adults. Electroencephalography and Clinical Neurophysiol. 105: 490-497.

Taborikova H. and Sax D.S., 1968. Motorneurone pool and the H-reflex. J. Neurol. Neurosurg. Psychiat. 31: 354-361.

Taborikova H. and Sax D.S., 1969. Conditioning of H-reflexes by a preceding subthreshold H-reflex stimulus. *Brain 92*: 203-212.

Whelan, P.J., Hiebert, G.W. and Pearson, K.G., 1995. Stimulation of the group I extensor afferents prolongs the stance phase in walking cats. *Exp. Brain Res. 103*: 20-30.

White S.C., Yack H.J., Tucker C.A. and Lin H.-Y., 1998. Comparison of vertical ground reaction forces during overground and treadmill walking. *Med. Sci. Sports Exerc. 30*(10): 1537-1542.